THE

PHYSIOLOGY OF MAN;

DESIGNED TO REPRESENT

THE EXISTING STATE OF PHYSIOLOGICAL SCIENCE,

AS APPLIED

TO THE FUNCTIONS OF THE HUMAN BODY.

BY

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PREFACE.

With the completion of this volume, all of the subjects belonging to human physiology, that are usually taught in medical schools or are treated of in systematic works, have been carefully considered, except the functions of the nervous system and the processes of generation and development. The first volume, published in 1866, treated of the blood, circulation, and respiration; and the second volume, published in 1867, was upon the subjects of alimentation, digestion, absorption, and the lymph and chyle.

The original plan of the work has been adhered to in the preparation of these three volumes, as each one constitutes a separate and distinct treatise, being complete in itself, while the full series is intended to cover the entire subject of human physiology. In recording the success of the parts already published, the author feels that his labors have been more than appreciated; and the friendly and encouraging criticism that the work has thus far received has stimulated him to increased efforts in the preparation of the present volume.

Some of the subjects taken up in this volume have an especial interest to the author, from the fact that he has

investigated them by original experiments, and has succeeded in developing new facts of a certain degree of value; but it has been his endeavor not to give to these questions undue prominence, to the prejudice of other subjects of equal importance to the physiological student. The most prominent points developed by original investigation in the present volume are, the discovery of an excretory function of the liver, that had never before been described, and the mechanism of glycogenesis, a question that seems now to be definitively settled, notwithstanding the apparently opposite results obtained by different experimenters.

Since the chapter on the glycogenic function of the liver has been printed, the author has seen an analysis of a series of observations on this subject, in which his conclusions with regard to the mechanism of the formation of sugar in the economy have been fully confirmed. The views embodied in this chapter, however, are entirely original, and were published in the *New York Medical Journal* in January, 1869.[1] The confirmatory observations, by Tieffenbach, are also original, as far as any knowledge of this publication is concerned, and were published in the form of an Inaugural Dissertation, later in the same year.[2] In laying claim to priority of publication, the author fully appreciates the importance of these independent experiments, by which the accuracy of his own researches have been so fully confirmed.

[1] FLINT, Jr., *Experiments undertaken for the Purpose of reconciling some of the Discordant Observations upon the Glycogenic Function of the Liver.—New York Medical Journal*, Jan., 1869, p. 373.

[2] TIEFFENBACH, *Ueber die Existenz der glycogenen Function der Leber, Dissertation*, Königsberg, 1869.—*Zeitschrift für rationelle Medicin*, Leipzig u. Heidelberg, 1869, Dritte Reihe, Bd. xxxv., S. 210.

With regard to the general mechanism of secretion, it has seemed important to the author to draw as closely as possible, the line of distinction between secretions proper and excretions; and our information with regard to the mode of formation of the secretions, and the production of excrementitious principles and their separation from the blood, is now of so positive a character, that we are able to subject these processes to pretty definite generalization.

If we comprehend fully the mechanism of secretion and excretion, it is evident that our knowledge of particular fluids must be to a great extent based upon accurate proximate analyses. The author has taken the greatest care in compiling the tables of composition of the various secretions and excretions, particularly with regard to the urine, having endeavored to make the table of its composition represent as closely as possible the general process of disassimilation and its variations under physiological conditions.

The author cannot but regard the description of the excretory function of the liver, with the discovery of the physiological relations of cholesterine, as of very great importance, in its relations to pathology as well as physiology. This subject has been elaborately considered in the chapter treating of the excretory function of the liver, and the views therein presented are put forward with more confidence, since they have been honored with a favorable report by a committee from the French *Academy of Sciences.*[1] As the result of the author's investigations on this subject, it seems to be conclusively proven that cholesterine, under certain

[1] St. Laugier, *Académie des sciences. Rôle de la cholestérine dans l'organisme, recherches de* M. Austin Flint (*fils*).—*Revue des cours scientifiques*, Paris, 1868-1869, tome vi., p. 495, and *Comptes rendus*, Paris, 1869, tome lxviii., p. 1371.

pathological conditions, bears the same relation to disorganizing diseases of the liver that urea does to corresponding conditions of the kidneys. The experiments by which these facts have been developed are so repulsive and difficult that there is little likelihood of their being extensively verified; and, while the author confidently awaits the time when the results of his investigations will be generally admitted, he is satisfied at present with the acknowledgment that they are entirely original.

Within a short time, several mooted points of great importance with regard to the physiological anatomy of the liver and the kidneys have been definitively settled. It is hoped that the chapters in which these anatomical questions have been considered will be found to represent the latest and most reliable views; and it does not seem now that the conclusions will be materially altered by future researches.

New York, September, 1869.

The present impression of this volume has been thoroughly and carefully revised, and contains numerous corrections and alterations. These have been made from time to time in the plates since the first publication of the volume, in 1869, and the full revision and correction have just been completed.

New York, September, 1874.

CONTENTS.

CHAPTER I.

SECRETION IN GENERAL.

CHAPTER II.

SEROUS AND SYNOVIAL FLUIDS—MUCUS—SEBACEOUS FLUIDS.

CHAPTER III.

MAMMARY SECRETION.

CHAPTER IV.

EXCRETION—ACTION OF THE SKIN.

CHAPTER V.

PHYSIOLOGICAL ANATOMY OF THE KIDNEYS.

CHAPTER XII.

NUTRITION.

CHAPTER XIII.

ANIMAL HEAT.

CHAPTER XIV.

SOURCES OF ANIMAL HEAT.

CHAPTER XV.

MOVEMENTS—GENERAL PROPERTIES OF CONTRACTILE TISSUES.

CHAPTER XVI.

MUSCULAR CONTRACTION—PASSIVE ORGANS OF LOCOMOTION.

CHAPTER XVII.

VOICE AND SPEECH.

LIST OF ILLUSTRATIONS.

PHYSIOLOGY OF MAN.

CHAPTER I.

SECRETION IN GENERAL.

General considerations—Relations of the secretions to nutrition—General mechanism of secretion—Differences between the secretions and fluids containing formed anatomical elements—Division of secretions—Mechanism of the production of the true secretions—Mechanism of the production of the excretions—Influence of the composition and pressure of the blood upon secretion—Influence of the nervous system on secretion—Excito-secretory system of nerves—General structure of secreting organs—Anatomical classification of glandular organs—Secreting membranes—Follicular glands—Racemose glands—Tubular glands—Ductless, or blood-glands—Classification of the secreted fluids—Secretions proper (permanent fluids; transitory fluids)—Excretions—Fluids containing formed anatomical elements.

THE phenomena classed by physiologists under the head of secretion are intimately connected with the general process of nutrition. In the sense in which the term secretion is usually received, it embraces most of the processes in which there is a separation of material from the blood or a formation of a new fluid out of matters furnished by the blood. The blood itself, with the lymph and the chyle, are no longer regarded as secretions. These fluids, like the tissues, are permanent constituents of the organism, undergoing those changes only that are necessary to their proper regeneration. They are likewise characterized by the presence of certain formed anatomical ele-

ments, which themselves undergo the processes of molecula destruction and regeneration. These characters are not pos sessed by the secretions. As a rule, the latter are homoge neous fluids, without formed anatomical elements, except a accidental constituents; such as the desquamated epithe lium in mucus or in sebaceous matter. The secretions are no permanent, self-regenerating fluids, except when they per form simply a mechanical function, as the humors of th eye, or the liquids in serous and synovial cavities. The are either discharged from the body, when they are calle excretions, or, after having performed their proper functio as secretions, are taken up again in a more or less modifie form by the blood.

With the exception of those fluids which have a functio almost entirely mechanical, the relations of the secretions t nutrition are so close, that the production of many of then forms almost a part of this great function. It is impossible for example, to conceive of nutrition without the formatio of the characteristic constituents of the urine, the bile, an the perspiration; and it is impossible, indeed, to study sati factorily the phenomena of nutrition without considerin fully the various excrementitious principles, such as urea cholesterine, creatine, creatinine, etc.; for the constant forma tion and discharge of these principles by disassimilatio create the necessity for the deposition of new matter i nutrition. Again, the most important of the secretions, a contradistinguished from the excretions, are concerned in th preparation of food by digestion, for the regeneration of th great nutritive fluid.

As would naturally be supposed, the general mechanism of secretion was very imperfectly understood early in th history of physiology, when little was known of the circula tion, the functions of the digestive fluids, and particularly o nutrition. From its etymology, the term should signif separation; but it is now known that many of the secrete fluids are formed in the glands, and are not simply sepa

rated, or filtered from the blood. Physiologists now regard secretion as the act by which fluids, holding certain solid principles in solution, and sometimes containing liquid nitrogenized principles, but not necessarily possessing formed anatomical elements, are separated from the blood, or are manufactured by special organs out of materials furnished by the blood. These organs may be membranes, follicles, or collections of follicles or tubes, when they are called glands. The liquids thus formed are called secretions; and they may be destined to perform some function connected with nutrition, or may be simply discharged from the organism.

It is not strictly correct to speak of formed anatomical elements as the results of secretion, except, perhaps, in the case of the fatty particles in the milk. The leucocytes found in pus, the spermatozoids of the seminal fluid, and the ovum, which are sometimes spoken of as products of secretion, are real anatomical elements developed in the way in which these structures are ordinarily formed. It has been conclusively demonstrated, for example, that leucocytes, or pus-corpuscles, are developed in a clear blastema, without the intervention of any special secreting organ;[1] and that spermatozoids and ova are generated by a true development in the testicles and the ovaries, by a process entirely different from ordinary secretion. It is important to recognize these facts in studying the mechanism by which the secretions are produced. It is true that in some of the secretions, as the sebaceous matter, a certain quantity of epithelium, more or less disintegrated, is found, but this is to be regarded as an accidental admixture of desquamated matter, and not as a product of secretion.

Division of Secretions.—The secretions are capable of a physiological division, dependent upon differences in their functions and the mechanism of their production. Investi-

[1] See vol. i., Blood, p. 124, and vol. ii., Absorption, p. 523.

gations within the past few years have shown that these differences are very distinct.

Certain of the fluids are formed by special organs, and have important functions to perform, which do not involve their discharge from the organism. These may be classed as the true secretions; and the most striking examples of them are the digestive fluids. Each one of these fluids is formed by a special gland or set of glands, which generally has no other function; and they are never produced by any other part. It is the gland which produces the characteristic element or elements of the true secretions out of materials furnished by the blood; and the principles thus formed never preëxist in the circulating fluid. The function which these fluids have to perform is generally intermittent; and when this is the case, the flow of the secretion is intermittent, taking place only when its action is required. When the parts which produce one of the true secretions are destroyed, as may be sometimes done in experiments upon living animals, the characteristic elements of this particular secretion never accumulate in the blood, nor are they formed vicariously by other organs. The simple effect of such an experiment is absence of the secretion, and the disturbances consequent upon the loss of its function.

Certain other of the fluids are composed of water, holding one or more characteristic principles in solution, which result from the physiological waste of the tissues. These principles have no function to perform in the animal economy, and are simply separated from the blood to be discharged from the body. These may be classed as excretions; the urine being the type of fluids of this kind. The characteristic principles of the excrementitious fluids are formed in the tissues, as one of the results of the constant nutritive changes going on in all organized living structures. They are not produced in the glands by which they are eliminated, but appear in the secretion as the result of a sort of elective filtration from the blood. They always preëxist in the circulating

fluid, and may be eliminated, either constantly or occasionally, by a number of organs. As they are produced continually in the substance of the tissues and taken up by the blood, they are constantly discharged into the substance of the proper eliminating organs. When the glands which thus eliminate these principles are destroyed, or their function seriously impaired, the excrementitious matters may accumulate in the blood, and give rise to certain toxic phenomena. These effects, however, are often retarded by the vicarious discharge of such principles by other organs.

There are some fluids, as the bile, which perform important functions as secretions, and which nevertheless contain certain excrementitious matters. In these instances it is only the excrementitious matters that are discharged from the organism.

In the serous sacs, the sheaths of tendons and of muscles, the substance of muscles, and some other situations, are found fluids which simply moisten the parts, and which contain very little organic matter and but a small proportion of inorganic salts. Although these are frequently spoken of as secretions, they are produced generally by a simple mechanical transudation of certain of the constituents of the blood through the walls of the blood-vessels.[1] Still, it is difficult to draw a line rigorously between transudation and some of the phenomena of secretion; particularly as late experiments upon dialysis have shown that simple osmotic membranes are capable of separating complex solutions, allowing certain constituents to pass much more freely than others.[2] This fact explains why the transuded fluids do not contain all the soluble principles of the blood in the proportions which exist in the plasma. All the secreted fluids, both the true secretions and the excretions, contain many of the inorganic salts of the blood-plasma.

[1] See vol. ii., Absorption, p. 505. [2] Ibid., p. 477.

Mechanism of the Production of the true Secretions.—Although the characteristic elements of the true secretions are not to be found in the blood or in any other of the animal fluids, they can generally be extracted in quantity from the glands, particularly during their intervals of repose. This fact has been repeatedly demonstrated with regard to many of the digestive fluids, as the saliva, the gastric juice, and the pancreatic juice; and artificial fluids, possessing many of the physiological properties of the natural secretions, have been prepared by simply infusing the glandular tissue in water. There can be no doubt, therefore, that even during the periods when the secretions are not discharged, the glands are taking from the blood matters which are to be transformed into principles characteristic of the individual secretions, and that this process is constant. Extending our inquiries into the nature of the process by which these peculiar principles are formed, it is found to bear a close resemblance to the general act of nutrition. There are certain anatomical elements in the glands which have the power of selecting the proper material from the blood and causing them to undergo a peculiar transformation; as the muscular tissue takes from the great nutritive fluid the albumen, fibrin, etc., and transforms them into its own substance. The exact nature of this property is unexplained; it belongs to the class of phenomena observed in living structures only, and is sometimes called vital.

In all of the secreting organs a variety of epithelium is found, called glandular, which seems to possess the power of forming the peculiar elements of the different secretions. Inasmuch as the epithelial cells lining the tubes or follicles of the glands constitute the only peculiar structures of these parts, the rest being made up of basement-membrane, connective tissue, blood-vessels, nerves, and other structures which are distributed generally in the economy, we should expect that these alone would contain the elements of the secretions. In all probability this is the fact; and with re-

gard to some of the glands, this has been satisfactorily demonstrated. It has been found, for example, that the liver-cells contain the glycogenic matter formed by the liver;[1] and it has been farther shown that when the cellular structures of the pancreas have been destroyed, the secretion is no longer produced.[2] There can be hardly any doubt with regard to the application of this principle to the glands generally, both secretory and excretory. Indeed, it is well known to pathologists, that when the tubes of the kidney have become denuded of their epithelium, they are no longer capable of separating from the blood the peculiar constituents of the urine.

With regard to the origin of the principles peculiar to the true secretions, it is impossible to entertain any other view than that they are produced in the epithelial structures of the glands; and the old idea that they exist ready-formed in the blood, though adopted by some physiologists of the present day,[3] cannot be maintained. While the secretions contain inorganic salts transuded in solution from the blood, the organic constituents, such as pepsin, ptyaline, pancreatine, etc., are readily distinguished from all other albuminoid principles by their peculiar physiological properties; although some of them are apparently identical with albumen in their ultimate composition and in most of their chemical reactions.

It may be stated, then, as a general proposition, that the characteristic elements of the true secretions, as contradistinguished from the excretions, are formed *de novo* by the epithelial structures of the glands, out of material furnished by the blood; and that their formation is by no means confined to what is usually termed the period of functional activity of the glands, or the time when the secretions are poured out,

[1] SCHIFF, *De la nature des granulations qui remplissent les cellules hépatiques: Amidon animale.—Comptes rendus*, Paris, 1859, tome xlviii., p. 880.

[2] BERNARD, *Mémoire sur le pancréas*, Paris, 1856, pp. 17 and 69.

[3] MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 282.

but takes place more or less constantly when no fluid is discharged.

It is more than probable that the formation of the elements of the secretions takes place with fully as much activity in the intervals of secretion as during the discharge of fluid; and most of the glands connected with the digestive system seem to require certain intervals of repose, and are capable of discharging their secretions for a limited time only.

When a secreting organ is called into functional activity—like the gastric mucous membrane, or the pancreas, upon the introduction of food into the alimentary canal—a marked change takes place. The circulation in the part is then very much increased in activity; thus furnishing the water and the inorganic elements of the secretion. This difference in the vascularity of the glands during their activity is very marked when the organs are exposed in a living animal, and is one of the important facts bearing upon the mechanism of secretion. Beaumont observed this in his experiments on St. Martin, and was the first to show conclusively that the gastric juice is secreted only when food is taken into the stomach, or some stimulation is applied to its mucous membrane.[1] Bernard, in his experiments on the pancreas, noted the pale appearance of the gland during the intervals of digestion, and its reddened and congested condition when the secretion flowed from the duct;[2] and these observations have been confirmed by all who have experimented upon the glands in living animals.

In later experiments upon the circulation in the salivary glands and its relation to secretion, Bernard has investigated this subject fully, with the most definite and satisfactory results.[3] His observations were made chiefly on the submaxil-

[1] BEAUMONT, *Experiments and Observations on the Gastric Juice, and the Physiology of Digestion*, Plattsburg, 1833, p. 103.

[2] BERNARD, *Mémoire sur le pancréas*, Paris, 1856, p. 43.

[3] BERNARD, *Leçons sur les propriétés physiologiques et les altérations patho*

lary gland in dogs; and he has shown that during the functional activity of this organ, if a tube be introduced into the vein, the quantity of blood which may be collected in a given time is four or five times that which is discharged in the intervals of secretion.[1] It was ascertained, also, that the venous blood coming from the gland contained much less water than the arterial blood; and on comparing the quantity of water lost by the blood in its passage through the gland in a given time with the quantity discharged in the saliva, they were found to exactly correspond.[2]

The differences in the quantity and the composition of the blood coming from the glands during their repose and their activity have an important bearing upon the mechanism of secretion. As far as the composition is concerned, these differences appear to be mainly dependent upon the modifications in the circulation. When the gland is in repose, the blood coming from it has the usual dark, venous hue and contains the ordinary proportion of carbonic acid; but during secretion, when the quantity of blood passing through the organ is increased, the color is nearly as bright as that of arterial blood, and the proportion of carbonic acid is very small. At this time, also, the blood is frequently discharged from the vein *pulsatim* to the distance of several inches.[3] The cause of this difference in color is very easily understood. During the intervals of secretion, the blood is sent to the gland for the purposes of nutrition and the manufacture of the elements of the secretion. It then passes

logiques des liquides de l'organisme, Paris, 1859, tome ii., p. 272, *et seq.*; *Du rôle des actions réflexes paralysantes dans le phénomène des sécrétions.—Journal de l'anatomie et de la physiologie*, Paris, 1864, tome i., p. 507, *et seq.*; *Leçons sur les propriétés des tissus vivants*, Paris, 1866, p. 400, *et seq.*

[1] Unpublished lectures delivered by Bernard at the College of France in the summer of 1861.

[2] Unpublished lectures, 1861; *Journal de l'anatomie et de la physiologie*, Paris, 1864, tome i., p. 513; and *Leçons sur les propriétés des tissus vivants*, Paris, 1866, p. 401.

[3] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 296.

through the part in moderate quantity and undergoes the usual change from arterial to venous, in which a great part of the oxygen disappears and carbonic acid is formed; but, when secretion commences, the ordinary nutritive changes are not sufficient to deoxidize the increased quantity of blood, and the venous character of the blood coming from the part is very much less marked.[1]

These facts enable us to form a pretty clear idea of the mechanism of secretion; though the exact nature of the forces which effect the changes of the organic principles of the blood into the characteristic elements of the secretions is not understood. Experiments, however, have shown that in the act of secretion there are two tolerably distinct processes:

1. It may be assumed that at all times the peculiar secreting cells of the glands are forming, more or less actively, the elements of the secretions, which may be washed out of the part or extracted by maceration; but during the intervals of secretion, the quantity of blood received by the glands is relatively small.

2. In obedience to the proper stimulus, when a gland takes on secretion, the quantity of blood which it receives is four or five times greater than it is during repose. At that time, water, with certain of the salts of the blood in solution, passes into the secreting structure, takes up the characteristic elements of the secretion, and fluid is discharged by the duct.

In all the secretions proper, there are intervals, either of complete repose, as is the case with the gastric juice or the pancreatic juice, or periods when the activity of the secretion is very greatly diminished, as in the saliva. These periods of repose seem to be necessary to the proper performance of the function of the secreting glands; forming a marked contrast with the constant action of the organs of excretion. It

[1] This subject is more fully discussed in vol. i., Blood, p. 106, under the head of "Color of the Blood."

is well known, for example, that the function of digestion is seriously disturbed when the act is too prolonged, from the habitual ingestion of an excessive quantity of food. With regard to the pancreas this fact has been demonstrated in the most satisfactory manner. The experiments of Bernard and others have shown that this organ is peculiarly susceptible to irritation; and when a tube is fixed in its duct, after a time the flow of the secretion may become constant, leaving no intervals for repose of the gland. When this occurs, the fluid discharged loses the character of the normal secretion and is found to possess none of its peculiar digestive properties.[1] In one or two instances in which the irritation of the tube introduced into the pancreatic duct did not produce a constant secretion, the fluid, which was discharged intermittently in the normal way, possessed all its physiological properties.[2]

From the considerations already mentioned, it is evident that the secretions, as the rule, are formed by the epithelial structures of the glands. There has been a great deal of speculation with regard to the mechanism of this action of the cells. As we before remarked, this question cannot be considered as settled. It does not seem probable that the cells are ruptured during secretion and discharge their contents into the ducts, for under these circumstances we should expect to find some of their structure in the secreted fluid; whereas, aside from accidental constituents, the secretions are homogeneous, and do not contain any formed anatomical elements. There is no good reason for supposing that this action takes place, and that more or less of the glandular epithelium is destroyed whenever secretion occurs; and, in the present state of our knowledge, we can only assume that the secreting cells induce certain transformations in the organic elements of the blood and modify transudation, without pretending to understand the exact nature of this process.

[1] See vol. ii., Digestion, p. 337.

[2] BERNARD, *Mémoire sur le pancréas*, Paris, 1856, p. 46.

The theory that the discharge of the secretions is due simply to mechanical causes, and is attributable solely to the increase in the pressure of blood, cannot be sustained. Pressure undoubtedly has considerable influence upon the activity of secretion; but the flow will not always take place in obedience to simple pressure, and secretion may be induced for a limited time without any increase in the quantity of blood circulating in the gland. In the numerous experiments by Bernard upon the influence of the circulation upon secretion in the submaxillary gland of the dog, these facts are very clearly shown. By very powerful galvanization of what he termed the motor nerve of the gland (the chorda tympani), secretion was excited, but the circulation was reduced; and again, after ligation of the vein, by which the gland was engorged with blood and the circulation could not be modified, galvanization of the nerve was nevertheless followed by an increase in the secretion. A slight secretion was also produced by galvanization of the nerve after the artery supplying the gland had been tied. These experiments are made with great facility upon the submaxillary gland of the dog, for the reason that the parts may be exposed and operated upon without interrupting the secretory function, and the nerves and vessels communicating with the gland can be easily isolated. The function of most of the glands, however, becomes so much disturbed by exposure, that the influence of the nerves upon their action is observed with great difficulty.

From the experiments just cited, Bernard concludes that the glands possess a peculiar irritability, which is manifested by their action in response to proper stimulation. During their secretion, they generally receive an increased quantity of blood; but this is not indispensable, and secretion may be excited without any modification of the circulation. This irritability will disappear when the artery supplying the part with blood is ligated for a number of hours; and secretion cannot then be excited, even when the motor nerve is stimu-

lated and the blood is again allowed to circulate. If the gland be not deprived of blood too long, the irritability is soon restored; but it may be permanently destroyed by depriving the part of blood for a long time.[1] These observations are very striking, and show a certain similarity between glandular and muscular irritability, though their properties are manifested in very different ways.

Mechanism of the Production of the Excretions.—Certain of the glands have the function of separating from the blood excrementitious matters, which are of no use in the economy, and are simply to be discharged from the system. These matters, which will be fully considered, both in connection with the fluids of which they form a part, and under the head of nutrition, are entirely different in their mode of production from the characteristic elements of the secretions. Our definite information concerning the mechanism of excretion dates from the researches of Prévost and Dumas, who discovered urea in the blood of dogs after its elimination had been arrested by extirpation of the kidneys.[2] These experiments were confirmed by Ségalas and Vauquelin;[3] but at that time the means of analysis of the animal fluids were not sufficiently delicate to enable chemists to detect urea in healthy blood. The later observations of Marchand, however, demonstrated its constant presence in very small quantity in the blood.[4] These analyses have been repeatedly confirmed, and it is now generally believed that all the excrementitious principles exist in greater or less quantity

[1] Unpublished lectures delivered by Bernard at the College of France in the summer of 1861.

[2] PRÉVOST ET DUMAS, *Examin du sang et de son action dans les divers phénomènes de la vie.—Annales de chimie et de physique*, Paris, 1821, tome xviii., p. 280.

[3] SÉGALAS, *Sur des nouvelles expériences relatives aux propriétés médicamenteuses de l'urée*, etc.—*Journal de physiologie*, Paris, 1822, tome ii., p. 354.

[4] MARCHAND, *Sur la présence de l'urée dans le sang.—Annales des sciences naturelles*, Paris, 1838, 2me série, tome x., p. 46.

in the circulating fluid.[1] That urea is actually separated from the blood by the kidneys is farther confirmed by recent observations, showing that in the renal artery the proportion of this principle is about twice as great as in the renal vein.[2]

Adopting this view, we have nothing to do at present with the formation of excrementitious principles. This takes place in the tissues and is connected with the general process of nutrition; and in the excreting glands there is simply a separation of matters already formed. The action of the excreting organs being constant, there is not that regular periodic increase in the activity of the circulation which is observed in secreting organs; but it has been observed that the blood that comes from the kidneys is nearly as red as arterial blood, showing that the quantity of blood which this organ receives is greater than is required for mere nutrition, the excess, as in the secreting organs, furnishing the water and inorganic salts that are found in the urine. It has also been shown that when the secretion of urine is interrupted, the blood of the renal veins becomes dark like the blood in the general venous system.[3]

The function of excretion is not, under all conditions, confined to the ordinary excretory organs. When their function is disturbed, certain of the secreting glands, as the follicles of the stomach and intestine, may for a time eliminate excrementitious matters; but this action is abnormal, and is

[1] In a recent work on the urine (ROBERTS, *A Practical Treatise on Urinary and Renal Diseases*, Philadelphia, 1866, p. 359), it is stated on the authority of observations and analyses by Oppler, Schottin, Perls, and Zalesky, that urea and uric acid are actually produced in the kidneys. These statements, which will be discussed more fully hereafter, are in direct opposition to facts that have been regarded as settled by accurate analyses of the blood, and cannot be accepted without confirmation. It is supposed, however, that urea and the urates are the result of transformation of other excrementitious principles existing in the blood, and are not formed *de novo*, like the elements of the true secretions.

[2] ROBIN, *Leçons sur les humeurs normales et morbides du corps de l'homme*, Paris, 1867, p. 89.

[3] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome i., pp. 257 and 297.

analogous to the elimination of foreign matters from the blood by the glands.

Influence of the Composition and Pressure of the Blood upon Secretion.—Under normal conditions the composition of the blood has little to do with the action of the secreting organs, as it simply furnishes the material out of which the characteristic principles of the secretion are formed; but when certain foreign matters are taken into the system or are injected into the blood-vessels, they are eliminated by the different glands, both secretory and excretory. These organs seem to possess a power of selection in the elimination of different substances. Thus, sugar, ferrocyanide of potassium, and the salts of iron, are eliminated in greatest quantity by the kidneys; the salts of iron by the kidneys and the gastric tubules; and iodine by the salivary glands.

The act of secretion is almost always accompanied with increase in the pressure of blood in the vessels supplying the glands; and it has been shown, on the other hand, that an exaggeration in the pressure, if the nerves of the glands do not exert an opposing influence, increases the activity of secretion. The experiments of Bernard on this point show the influence of pressure on the salivary and the renal secretion, particularly the latter. After inserting a tube into one of the ureters of a living animal, so that the activity of the renal secretion could be accurately observed, the pressure in the renal artery was increased by tying the crural and the brachial. It was then found that the flow of urine was markedly increased. The pressure was afterward diminished by the abstraction of blood, which was followed by a corresponding diminution in the quantity of urine.[1] The same phenomena were observed in analogous experiments on the submaxillary secretion.

These striking facts, as we have already seen, do not demonstrate that secretion is due simply to an increase in the

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 155, *et seq.*

pressure of blood in the glands, though this undoubtedly exerts an important influence. It is necessary that every condition should be favorable to the act of secretion, for this influence to be effective. Experiments have shown that pain is capable of completely arresting the secretion of urine; operating undoubtedly through the nervous system. If, now, the flow of urine be arrested by pain, an increase in the pressure of blood in the part fails to influence the secretion. To illustrate this fact more fully, Bernard divided the nerves on one side, through which the reflex nervous action was communicated to the kidney, leaving the other side intact. He then found that increase in the arterial pressure, accompanied with pain, diminished the flow of urine on the sound side, through which the nervous action could operate, and increased it upon the other.[1] We have already alluded to the experiments in which secretion was excited through the nervous system, when the arterial pressure had been considerably diminished.

The influence of pressure of blood upon secretion may, then, be summed up in a few words: There is always an increase in the activity of secretion when the pressure of blood in the glands is increased, and a diminution when the pressure is reduced; except when there is some modifying influence operating through the nervous system.

Influence of the Nervous System on Secretion.—The fact that the secretions are generally intermittent in their flow, being discharged in obedience to impressions which are made only when there is a demand for the exercise of their functions, would naturally lead to the supposition that they are regulated, to a great extent, through the nervous system; particularly as it is now well established that the nerves are capable of modifying and regulating local circulations. The same facts apply, to a certain extent, to the excretions, which

[1] These experiments were detailed by Bernard in his lectures at the College of France in the summer of 1861.

are also subject to considerable modifications. A few years ago, indeed, there was considerable discussion regarding a subdivision of the reflex system of nerves, which was supposed to preside over secretion, and was called the excito-secretory system. The facts which led to the description of this system of nerves had long been observed; and they simply illustrated the production of secretion in response to irritation. Dr. H. F. Campbell, of Augusta, Georgia, published, in 1857, an essay on the excito-secretory system of nerves, which received the prize of the American Medical Association for that year;[1] and a few months later, the same idea was put into shape by Dr. Marshall Hall, who, however, yielded the priority to Dr. Campbell. To Dr. Campbell certainly belongs the credit of proposing the theory that the sympathetic system presides over secretion; but in this he only reasoned from the old experiments of Pourfour du Petit and others, and failed to give any satisfactory physiological demonstration of his views.

In 1852, five years before the publication of Dr. Campbell's essay, in the course of his researches on the secretions of the different salivary glands, Bernard pointed out the reflex character of the act of secretion, and demonstrated experimentally the influence of certain nerves upon the discharge of fluid from the duct of the submaxillary. These experiments were the first to give a clear idea of the action of the nervous system upon secretion, and they have been

[1] CAMPBELL, *Essays on the Secretory and the Excito-secretory System of Nerves in their Relations to Physiology and Pathology*, Philadelphia, 1857; also, *Transactions of the American Medical Association* for 1857.

In 1850, Dr. Campbell published in the *Southern Medical and Surgical Journal* an *Essay on the Influence of Dentition in producing Disease;* in which he remarked the fact, that during dentition, the irritation in the mouth frequently induced, in addition to the usual increase in the salivary secretions, an increased action of the kidneys and the mucous membrane of the intestinal canal. He states that "this increase and change in the secretion are effected by the agency of the altered function of the nerve upon the arteries from which these secretions are eliminated." Dr. Campbell supposed that the nerves through which these operations took place belonged to the sympathetic system.

confirmed and extended by the subsequent observations of Bernard and other physiologists. The following are the most important facts, taken from Bernard, bearing upon the question under consideration:[1]

"Introducing into the mouth of a dog, in which the three salivary ducts have been isolated, a very sapid substance, such as vinegar, for example, it is found that the duct of the submaxillary discharges saliva in very great abundance. But, by operating directly upon the nerve of taste itself, I have been enabled to act solely upon the special secretion, and to demonstrate directly this intimate relation between the secretion of the submaxillary saliva and the sense of gustation.

"When we divide in a dog the lingual nerve opposite the middle of the horizontal process of the lower jaw, and pinch the central end, which is connected with the encephalon, we immediately see the duct of the submaxillary excrete saliva with great activity, while the ducts of the parotid and sublingual, which are not connected with the sense of gustation, remain perfectly dry. This sort of functional reaction, which irritation of the central end determines exclusively, in the submaxillary gland, is explained, for in operating thus we produce in the nervous centre the impression of exaggerated gustatory sensation, which immediately provokes, by an action called reflex, the salivary secretion destined physiologically to allay and diminish the too acute impression of sapid substances."

These experiments clearly demonstrated the importance of the nervous influence in the production of the secretions; but the more recent observations of Bernard show that the effects are produced mainly by increasing the activity of the circulation in the glands. This takes place in greatest part through filaments from the sympathetic system, which are

[1] BERNARD, *Recherches d'anatomie et de physiologie comparée sur les glandes salivaires chez l'homme et les animaux vertébrés.*—*Comptes rendus*, Paris, 1852, tome xxxiv., p. 239.

distributed to the muscular coats of the arteries of supply. When these filaments are divided, the circulation is increased here, as in other situations, and secretion is the result; and, if the extremity of the nerve connected with the gland be galvanized, contraction of the vessels follows, and the secretion is arrested.[1]

With regard to many of the glands, Bernard has shown that the influence of the sympathetic is antagonized by nerves derived from the cerebro-spinal system, which he calls the motor nerves of the glands. The motor nerve of the submaxillary is the chorda tympani; and as both this nerve and the sympathetic, together with the excretory duct of the gland, can be easily exposed and operated upon in a living animal, most of the experiments of Bernard have been performed upon this gland. When all these parts are exposed and a tube introduced into the salivary duct, division of the sympathetic induces secretion, with an increase in the circulation in the gland, the blood in the vein becoming red. On the other hand, division of the chorda tympani, the sympathetic being intact, arrests secretion, and the venous blood coming from the gland becomes dark. If the nerves be now galvanized alternately, it will be found that galvanization of the sympathetic produces contraction of the vessels of the gland and arrests secretion, while the stimulus applied to the chorda tympani increases the circulation and excites secretion.[2]

These experiments show that the submaxillary gland has distributed to it a special nerve which is capable of exciting its functional activity, the sympathetic ramifying upon the walls of the blood-vessels in this, as in other situations; and it remains to see whether other glands are likewise supplied with motor nerves. In his lectures, delivered in 1861, Bernard announced that he had demonstrated the existence of such nerves for the other salivary glands.

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 270.
[2] *Op. cit.*, p. 267, *et seq.*

The motor nerve of the parotid is derived from the auriculo-temporal branch of the submaxillary division of the fifth pair; and the nerve of the sublingual, from the lingual branch of the fifth. He found, however, that neither the parotid nor the sublingual was so easily excited to secretion by galvanization of the nerves as the submaxillary. With regard to other glands, the conditions for experimentation are so difficult, and some of them, as the pancreas, are so sensitive to irritation, that it is impossible to repeat on them the experiments made upon the salivary glands. Enough is known, however, of the nervous influences which modify secretion, to admit of the inference that all the glands are possessed of nerves through which reflex phenomena, affecting their secretions, take place. It is the motor, or functional nerve of the gland through which the reflex action takes place; the influence of the sympathetic being constant, and the same as in other parts where it is distributed to blood-vessels.

As reflex phenomena involve the action of a nervous centre, it becomes an interesting question to determine whether any particular parts of the central nervous system preside over the various secretions. We must refer again to the experiments of Bernard for an elucidation of this question. If a puncture be made in the space included between the origin of the pneumogastrics and the auditory nerves in the floor of the fourth ventricle, there is an increase in the discharge of urine, and an excretion of sugar, from an exaggeration in the sugar-producing function of the liver. Irritation applied a little higher, toward the pons Varolii, just posterior to the origin of the fifth pair of nerves, is followed by a great increase in the activity of the salivary secretion.[1]

[1] BERNARD, *Leçons sur la physiologie et la pathologie du système nerveux*, Paris, 1858, tome i., pp. 398–399.

This operation is easily performed upon the rabbit, by passing an instrument directly through the occipital bone, entering just behind the protuberance, and through the cerebellum to the medulla oblongata. These experiments will be more fully described in connection with the nervous system.

Mental emotions, pain, and various circumstances, the influence of which upon secretion has long been observed, operate through the nervous system. Numerous familiar instances of this kind are quoted in works on physiology: such as the secretion of tears; arrest or production of the salivary secretions; sudden arrest of the secretion of the mammary glands, from violent emotion; increase in the secretion of the kidneys or of the intestinal tract, from fear or anxiety; with other examples which it is unnecessary to ennumerate.

The effects, upon some of the secretory organs, of destruction of the nerves distributed to their parenchyma are very curious and interesting. Müller and Peipers destroyed the nerves distributed to the kidney, and found that not only was the secretion arrested in the great majority of instances, but that the tissue of the kidneys became softened and broken down.[1] These experiments have been lately repeated by Bernard. He found that animals operated upon in this way died, and that the tissue of the kidney was broken down into a fetid, semifluid mass. After division of the nerves of the salivary glands, the organs became atrophied, but did not undergo the peculiar putrefactive change which was observed in the kidneys. The same effect was produced when the nerve was paralyzed by introducing a few drops of a solution of woorara at the origin of the little artery which is distributed to the submaxillary gland.[2]

General Structure of Secreting Organs.—In treating of the mechanism of secretion and excretion, it has been evident that all glandular organs must be supplied with blood to furnish the materials for secretion, and be provided with epithelium, which changes these matters into the characteristic elements of the secretions. We can understand how cer-

[1] MUELLER, *Manuel de physiologie*, Paris, 1851, tome i., p. 391.

[2] BERNARD, *Leçons sur les propriétés des tissus vivants*, Paris, 1866, p. 399.

tain of the liquid and saline constituents of the blood can escape by exosmosis through the homogeneous walls of the capillaries,[1] but the more complex fluids require for their formation a different kind of action; although, in the act of secretion, there is considerable transudation of liquid and saline matters, which take up in their course the peculiar principles formed by the cells.

Though it is somewhat difficult to draw a line between transudation and the simplest forms of secretion, it may be assumed, in general terms, that fluids which are exhaled directly from the blood-vessels, without the intervention of glandular apparatus or of a secreting membrane, are transudations; while all fluids produced by simple membranes, by follicles, or discharged from the ducts of glands, are secretions. This division places the intermuscular fluid and the fluid found in all soft tissues among the transudations, and the serous and synovial fluids among the secretions.

The serous and synovial membranes present the simplest form of a secreting apparatus. Blood is supplied to them in small quantity, and on their free surfaces are arranged one or two layers of epithelial cells which effect the slight changes that take place in the transuded fluids. In some of the serous membranes, as the pleura and peritoneum, the amount of secretion is very small, being hardly more than a vaporous exhalation; but others, like the serous pericardium and the synovial membranes, secrete a considerable quantity of fluid. The action of all of these membranes may become exaggerated, as a pathological condition, and the amount of their secretions is then very large.

Anatomists have now a pretty clear idea of the structure of what are called the glandular organs; and it will be seen that they simply present an arrangement by which the secreting surface is increased, and at the same time compressed, as it were, into a comparatively small space. The mucous follicles, for example, are simple inversions of a portion of

[1] See vol. ii., Absorption, p. 505.

the mucous membrane; while the ordinary racemose glands are nothing more than collections of follicles around the extremities of excretory ducts. These ideas concerning the general anatomy of the glands date from the observations of Malpighi,[1] who was the first to correct the old notion that the secretions were discharged into the glandular organs through openings in the blood-vessels. It is evident that nothing could have been known of the mechanism of secretion before the connection between the arteries and veins had been ascertained, which, it will be remembered, was also discovered by Malpighi. Although the ideas of Malpighi were not at first generally received, more recent observations with the microscope have shown that they were in the main correct; though, from the imperfection of his optical instruments, Malpighi was unable to investigate the minute structure of the glands very thoroughly.

Anatomical Classification of Glandular Organs.—The organs which produce the different secretions are susceptible of a classification according to their anatomical peculiarities, which greatly facilitates their study. They may be divided as follows:

1. *Secreting membranes.*—Examples of these are the serous and synovial membranes.

2. *Follicular glands.*—Examples of these are the simple mucous follicles, the follicles of the stomach, the follicles of Lieberkühn, and the uterine follicles.

3. *Tubular glands.*—Examples of these are the ceruminous glands, the sudoriparous glands, and the kidneys.

4. *Racemose glands, simple and compound.*—Examples of the simple racemose glands are the sebaceous and Meibomian glands, the tracheal glands, and the glands of Brunner. Examples of the compound racemose glands are the salivary

[1] MALPIGHI, *Exercitationes Anatomicæ de Structura Viscerum.—Opera Omnia, Lugd.* Batav., 1687, tomus ii., p. 257.

glands, the pancreas, the lachrymal glands, and the mammary glands.

5. *Ductless, or blood-glands.*—Examples of these are the thymus, the thyroid, the supra-renal capsules, and the spleen.

The liver is a glandular organ which cannot be placed in any one of the above subdivisions, as we shall see when we treat specially of its anatomy. The lymphatic glands and other parts connected with the lymphatic and the lacteal system are not embraced in the above classification.[1] These are sometimes called conglobate glands.

The general structure of secreting membranes and the follicular glands is very simple. The secreting parts consist of a membrane, generally homogeneous, on the secreting surface of which are found epithelial cells, either tesselated or of the variety called glandular. Beneath this membrane ramify the blood-vessels which furnish the elements of the secretions. The follicles are simply digital inversions of this structure, with rounded, blind extremities, the glandular epithelium lining the tube.

The tubular glands have essentially the same structure as the follicles, except that the tubes are long and more or less convoluted. The more complex of these organs contain connective tissue, blood-vessels, nerves, and lymphatics.

The compound racemose glands are composed of branching ducts, around the extremities of which are arranged collections of rounded follicles, like bunches of grapes. In addition to the epithelium, basement-membrane, and blood-vessels, these organs contain connective tissue, fibro-plastic elements, lymphatics, involuntary muscular fibres, and nerves. In the simple racemose glands the excretory duct does not branch.

The ductless glands contain blood-vessels, lymphatics, nerves, sometimes involuntary muscular fibres, fibro-plastic elements, and a peculiar structure called pulp, which is com-

[1] For the anatomy of the lymphatic system, see vol. ii., Absorption, p. 439, *et seq.*

posed of fluid with cells and occasionally closed vesicles. These are sometimes called blood-glands, because they are supposed to modify the blood as it passes through their substance.

The testicles and the ovaries are not simple glandular organs; for in addition to the production of mucous or watery secretions, their principal function is to develop certain anatomical elements, the spermatozoids and the ova. The physiology of these organs will be considered in connection with the subject of generation.

Classification of the Secreted Fluids.—The products of the various glands may be divided, according to their function, into secretions and excretions. The secreted fluids may be subdivided into the permanent secretions, which have a more or less mechanical function, and transitory secretions; some of the latter, like mucus, are thrown off in small quantity, without being actually excrementitious; others, like most of the digestive fluids, are produced intermittently and rapidly, and finally undergo resorption.

Tabular View of the Secreted Fluids.

SECRETIONS PROPER.

Permanent Fluids.

Serous fluids.
Synovial fluid.
Aqueous humor of the eye.
Vitreous humor of the eye.
Fluid of the labyrinth of the internal ear.
Cephalo-rachidian, or subarachnoid fluid.

Transitory Fluids.

Mucus, in many varieties.
Sebaceous matter.
Cerumen, the waxy secretion of the external meatus.
Meibomian fluid.
Milk and colostrum.
Tears.
Saliva.

Gastric juice.
Pancreatic juice.
Secretion of the glands of Brunner.
Secretion of the follicles of Lieberkühn.
Secretion of the follicles of the large intestine.
Bile (also an excretion).

EXCRETIONS.

Perspiration, and the secretion of the axillary glands.
Urine.
Bile (also a secretion).

FLUIDS CONTAINING FORMED ANATOMICAL ELEMENTS.

Seminal fluid, containing, beside spermatozoids, the secretions of a number of glandular structures.
Fluid of the Graafian follicles.

CHAPTER II.

SEROUS AND SYNOVIAL FLUIDS—MUCUS—SEBACEOUS FLUIDS.

Physiological anatomy of the serous and synovial membranes—Synovial fringes—Bursæ—Synovial sheaths—Pericardial, peritoneal, and pleural secretions—Quantity of the serous secretions—Synovial fluid—Mucus—Mucous membranes—Mucous membranes covered with pavement-epithelium—Mucous membranes covered with columnar epithelium—Mucous membranes covered with mixed epithelium—Mechanism of the secretion of mucus—Composition and varieties of mucus—Microscopical characters of mucus—Nasal mucus—Bronchial and pulmonary mucus—Mucus secreted by the lining membrane of the alimentary canal—Mucus of the urinary passages—Mucus of the generative passages—Conjunctival mucus—General function of mucus—Non-absorption of certain soluble substances, particularly venoms, by mucous membranes—Sebaceous fluids—Physiological anatomy of the sebaceous, ceruminous, and Meibomian glands—Ordinary sebaceous matter—Smegma of the prepuce and of the labia minora—Vernix caseosa—Cerumen—Meibomian secretion—Function of the Meibomian secretion.

Physiological Anatomy of the Serous and Synovial Membranes.

THE serous and synovial membranes, which are frequently classed together by anatomists, present several well-marked points of distinction, both as regards their structure and the products of their secretion. The serous membranes are the arachnoid, pleura, pericardium, peritoneum, and tunica vaginalis testis. The synovial membranes are found around all the movable articulations. They also form elongated sacs enveloping many of the long tendons, and exist in various parts of the body in the form of shut sacs, when they are called bursæ.

Serous Membranes.—The structure of the serous membranes is very simple. They consist of a dense tissue of fibres, which is frequently quite closely adherent to the subjacent parts, and covered by a single layer of pavement, or tesselated epithelium. The fibres are mainly of the inelastic variety arranged in bundles, interlacing each other in the form of a close net-work, and mingled with small, wavy fibres of elastic tissue and numerous blood-vessels. It has not been satisfactorily demonstrated that the serous membranes contain nerves and lymphatics, though the latter are generally quite abundant in the subjacent parts, particularly beneath the visceral layers.[1] The capillary blood-vessels are in the form of a close, polygonal net-work, with sharp angles.

The epithelium of the serous membranes is pale, regular, with rather large nuclei, and is easily detached after death. Todd and Bowman describe a delicate basement-membrane between the fibrous structure and the layer of epithelium,[2] but others have not been able to distinguish it, and the existence of such a membrane is considered doubtful.[3]

These membranes, as a rule, form closed sacs, with their opposing or free surfaces nearly in apposition. The secretion, which is generally very small in quantity, is contained in their cavity. The exceptions to this are the arachnoid membrane, the surfaces of which are exactly in apposition, the fluid being situated beneath both layers,[4] and the peritoneum of the female, which has an opening on either said for the Fallopian tubes.

Synovial Membranes.—The true synovial membranes are found in the diarthrodial, or movable articulations; but in

[1] See vol. ii., Absorption, p. 433.

[2] Todd and Bowman, *Physiological Anatomy and Physiology of Man*, London, 1845, vol. i., p. 130.

[3] Brinton, *Serous and Synovial Membranes.—Cyclopædia of Anatomy and Physiology*, London, 1847–1849, vol. iv., part i., p. 514.

[4] Magendie, *Mémoire sur un liquide qui se trouve dans le crane et le canal vertébral de l'homme et des animaux mammifères.—Journal de physiologie*, Paris, 1825, tome v., p. 36.

various parts of the body are found closed sacs, sheaths, etc., which resemble synovial membranes both in structure and function. Every movable joint is enveloped in a capsule which is closely adherent to the edges of the articulating cartilage and is even reflected upon its surface for a short distance. It was formerly thought that these membranes, like the serous sacs, were closed bags, with one layer attached to the cartilage, and the other passing between the bones so as to enclose the joint; but it is now the general opinion that the cartilage which encrusts the articulating extremities of the bones, though bathed in synovial fluid, is not itself covered by a membrane.

The fibrous portion of the synovial membranes is more dense and resisting and less elastic than the serous membranes. It is composed of white inelastic fibrous tissue, with a few elastic fibres and blood-vessels. The latter are generally not so numerous as in the serous membranes. The internal surface is lined with small cells of flattened, pavement-epithelium, with rather large, rounded nuclei. These cells exist in from one to two or four layers.[1]

In most of the joints, especially those of large size, as the knee and hip, the synovial membrane is thrown into folds which contain a considerable amount of true adipose tissue. In nearly all the joints, the membrane presents fringed, vascular processes, called sometimes synovial fringes. These are composed of looped vessels of considerable size; and when injected they bear a certain resemblance to the choroid plexus. The edges of these fringes present numerous leaf-like, membranous appendages, of a great variety of curious forms. They are generally situated near the attachment of the membrane to the cartilage. There is no reason for supposing that either the adipose folds or the vascular fringes have any special office in the production of the synovial secretion, different from that of other portions of the membrane, though such a theory has been advanced.

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 201.

The arrangement of the synovial bursæ is very simple. Wherever a tendon plays over a bony surface, we find a delicate membrane in the form of an irregularly-shaped, closed sac, one layer of which is attached to the tendon, and the other to the bone. These sacs are lined with an epithelium like that found in the synovial cavities, and they secrete a true synovial fluid. Numerous bursæ are also found beneath the skin, especially in parts where the integument moves over bony prominences, as the olecranon, the patella, and the tuberosities of the ischium. These sacs, sometimes called bursæ mucosæ, are much more common in man than in the inferior animals, and have essentially the same function as the deep-seated bursæ. The form of both the superficial and deep-seated bursæ is very irregular, and their interior is frequently traversed by small bands of fibrous tissue. The synovial sheaths, or vaginal processes, line the canals in which the long tendons play, particularly the tendons of the flexors and extensors of the fingers and toes. They have essentially the same structure as the bursæ, and present two layers, one of which lines the canal, while the other is reflected over the tendon. The vascular folds, described in connection with the articular synovial membranes, are found in many of the bursæ and synovial sheaths.

Pericardial, Peritoneal, and Pleural Secretions.—In the normal condition of the true serous membranes, the amount of secretion is very small; so small, indeed, that it never has been obtained in quantity sufficient for ultimate analysis. It is not true that these membranes produce merely a vaporous exhalation. Their secretion is always liquid, and, small as it is in quantity, it can be found in the pericardial sac, and sometimes in the lower part of the abdominal cavity. As the only apparent function of these fluids is to moisten the membranes, so that the opposing surfaces can move over each other without undue fric-

tion, only enough fluid is secreted to keep these surfaces in a proper condition. The error frequently committed by authors, in describing the serous exhalations as vaporous, is due to the fact that a vapor is generally given off when the serous cavities are exposed, either in a living animal or in one recently killed. This vaporous exhalation takes place after exposure of the parts; but if the cavities be observed without exposing the serous surfaces to the air, a certain quantity of liquid can be detected. Colin always found liquid in the peritoneal, pericardial, and pleural cavities of animals recently killed or opened during life. In these cavities the opposite surfaces of the serous membrane were either in contact, or the space between them was filled with liquid. In one of the small ruminants, he removed the muscles and the elastic tunic from the lower part of the abdomen, exposing the transparent peritoneum, and through this membrane could see liquid collected in the dependent parts.[1]

As far as has been ascertained, the secretions of the different serous membranes bear a close resemblance to each other. They are either colorless, or of a slight amber tinge, alkaline in reaction, and have a specific gravity of from 1012 to 1020. Their composition resembles that of the serum of the blood, except that the proportion of water is very much greater. They contain albumen, chlorides, carbonate and phosphate of soda, and a little glucose. These facts are the result of observations upon the serous fluids of some of the inferior animals;[2] and it is exceedingly difficult to obtain the normal fluids from the human subject. The elaborate analyses which are sometimes given of the fluids from the different serous cavities in the human subject are the results of examinations of large morbid accumulations.[3]

[1] Colin, *Traité de physiologie comparée des animaux domestiques*, Paris, 1856, tome ii., p. 438.

[2] Colin, *loc. cit.*

[3] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 262, *et seq.* This author

The normal quantity of pericardial fluid in the human subject is generally estimated at from one to two fluidrachms. Colin found that the pericardial sac of the horse contained from two and a half to three and a half fluidounces, the cavity being exposed immediately after the death of the animal from hæmorrhage.

The quantity of fluid found in the peritoneal cavity in horses killed in this way was from ten to thirty-four fluidounces.

The quantity of fluid in the pleural cavity in the same animal was from three and a half to seven fluidounces.[1]

These estimates are simply approximative; but they give an idea of the normal quantity of liquid which may reasonably be supposed to exist in the serous cavities of the human subject. Judging from the weight of a man of ordinary size as compared with that of a horse, it may be stated, in general terms, that the pericardial sac contains from two and a half to three and a half fluidrachms; the peritoneal cavity from one to four fluidounces; and the pleural sac from three and a half to seven fluidrachms.

The fluid in the cavity of the tunica vaginalis is small in quantity, and resembles in every respect the peritoneal secretion. The cephalo-rachidian, or subarachnoid fluid will be described in connection with the anatomy of the cerebrospinal nervous system.

Synovial Fluid.—Although there is a certain similarity between the serous and the synovial membranes, their secretions differ very considerably in their physical and chemical characters. Like the serosities, the synovial fluid has simply a mechanical function; but it is more viscid, and contains a larger proportion of organic matter than the serous fluids. The quantity of fluid in the joints is sufficient to lubricate

has collected the latest analyses of the pleural fluid, the pericardial fluid, the fluid of ascites, and the fluid of hydrocele.

[1] COLIN, *loc. cit.*

freely the articulating surfaces. In a horse of medium size and in good condition, examined immediately after death, Colin found 1·6 fluidrachms in the shoulder-joint; 1·9 drachms in the elbow-joint; 1·6 drachms in the coxo-femoral articulation; 2·2 in the femoro-tibial; and 1·9 in the tibio-tarsal.[1]

When perfectly normal, the synovial fluid is either colorless or of a pale yellowish tinge. It is so viscid that it is with difficulty poured from one vessel to another. This peculiar character is due to the presence of an organic substance called synovine. When this organic matter has been extracted and mixed with water, it gives to the fluid the peculiar viscidity of the synovial secretion. The reaction of the fluid is faintly alkaline, on account of the presence of a small proportion of carbonate of soda. The fluid, especially when the joints have been much used, usually contains in suspension pale epithelial cells and a few leucocytes. The following is the composition of the synovial fluid of the human subject:[2]

Composition of the Synovial Fluid.

Water	928·00
Synovine (called albumen)	64·00
Principles of organic origin (belonging to the second class of Robin)	not estimated.
Fatty matter	0·60
Chloride of sodium, Carbonate of soda	6·00
Phosphate of lime	1·50
Ammonio-magnesian phosphate	traces.

The observations of Frerichs indicate considerable variations in the composition and general characters of the synovial fluid, dependent upon use of the joints. In a stall-fed ox the proportion of water to solid matter was 969·90 to 30·10; and in animals that took considerable exercise,

[1] Colin, *op. cit.*, tome ii., p. 440.
[2] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 276.

the proportions were 948·54 of water to 51·46 of solid matter. In the latter the fluid was more viscid, and contained a larger proportion of synovine with a smaller proportion of salts. It was also more deeply colored, and contained a larger number of leucocytes.[1]

Like the serous fluids, the synovial secretion is produced by the general surface of the membrane and not by any special organs. The folds and fringes which have been described were supposed at one time to be most active in secreting the organic matter, but there is no evidence that they have any such office.

The aqueous humor of the eye and the fluid found in the labyrinth of the internal ear resemble the serous secretions in many regards; but these fluids, with the vitreous humor, will be considered in connection with the physiological anatomy of the eye and the ear.

Mucus.

Mucous Membranes.—The mucous membranes in different situations present important peculiarities in structure, many of which have already been considered. We have described, in detail, in the preceding volumes, the mucous membrane of the air-passages and of the alimentary canal, in connection with the subjects of respiration and digestion; and the membranes in other parts will necessarily be described in treating of the physiology of the organs in which they are found. It will be sufficient at present to take a general view of the structure of these membranes and the mechanism of the production of the various fluids known under the name of mucus.

A distinct anatomical division of the mucous membranes may be made into two classes, as follows: First, those provided with pavement-epithelium; and second, those provided

[1] FRERICHS, in WAGNER, *Handwörterbuch der Physiologie*, Braunschweig, 1846, Band iii., S. 467.

with columnar, or conoidal epithelium. All of the mucous membranes line cavities or tubes communicating with the exterior by the different openings in the body.

The following are the principal situations in which the first variety of mucous membranes, covered with pavement-epithelium, are found: The mouth, the lower part of the pharynx, the œsophagus, the conjunctiva, the female urethra, and the vagina. In these situations the membrane is composed of a chorion made up of inelastic and elastic fibrous tissue, a few fibro-plastic elements, with capillaries, lymphatics, and nerves. The elastic fibres are small and quite abundant. The membrane itself is loosely united to the subjacent parts by areolar tissue. The chorion is provided with vascular papillæ, more or less marked; but in all situations, except in the pharynx, the epithelial covering fills up the spaces between these papillæ, so that the membrane presents a smooth surface. Between the chorion and the epithelium, is an amorphous basement-membrane. The mucous glands open upon the surface of the membrane by their ducts, but the glandular structure is situated in the submucous areolar tissue. These glands have many of them been described in connection with the mucous membrane of the mouth, pharynx, and œsophagus.[1] They are generally simple racemose glands, presenting a collection of follicles arranged around the extremity of a single excretory duct, lined or filled with rounded, nucleated epithelium.

The pavement-epithelium covering these membranes exists generally in several layers, and presents great variety, both in form and size. The most superficial layers are of large size, flattened, and irregularly polygonal. The deeper layers are smaller and more rounded. The size of these cells is from $\frac{1}{1500}$ to $\frac{1}{300}$ of an inch. The cells are pale, slightly granular, and possess a small, ovoid nucleus, with one or two nucleoli.

The second variety of mucous membranes, covered with

[1] See vol. ii., Digestion, p. 166.

columnar epithelium, is found lining the alimentary canal below the cardiac orifice of the stomach, the biliary passages, the excretory ducts of all the glands, the nasal passages, the upper part of the pharynx, the uterus and Fallopian tubes, the bronchi, the Eustachian tubes, and the male urethra. In certain situations this variety of epithelium is provided on its free surface with little hair-like processes called cilia. During life the cilia are in constant motion, producing a current generally in the direction of the mucous orifices. Ciliated epithelium is found throughout the nasal passages, commencing about three-quarters of an inch within the nose; the upper part of the pharynx; the posterior surface of the soft palate; the Eustachian tube; the tympanic cavity; the larynx, trachea, and bronchial tubes, until they become less than $\frac{1}{50}$ of an inch in diameter; the neck and body of the uterus; the Fallopian tubes; the internal surface of the eyelids, and the ventricles of the brain.

This variety of mucous membrane is formed of a chorion, a basement-membrane, and epithelium. The chorion is composed of inelastic and elastic fibres, with fibro-plastic elements, a few unstriped muscular fibres, amorphous matter, vessels, nerves, and lymphatics. It is less dense and less elastic than the chorion of the first variety, and is generally more closely united to the subjacent tissue. The surface of these membranes is generally smooth, the only exception being the mucous membrane of the pyloric portion of the stomach and the small intestines.

These membranes are provided with follicular glands, extending through their entire thickness and terminating in rounded extremities, sometimes single and sometimes double, which rest upon the submucous structure. Many of them are provided also with simple racemose glands, the ducts passing through the membrane, the glandular structure being situated in the submucous areolar tissue.[1]

[1] See vol. i., Respiration, p. 361, for a description of the glandular organs

The columnar epithelium covering these membranes rests upon an amorphous structure, called basement-membrane. It generally presents but few layers, and sometimes, as in the intestinal canal, there is only a single layer. The cells are prismoidal, with a large free extremity, and a pointed end which is attached. The lower strata of cells are shorter and more rounded than those in the superficial layer. The cells are pale, very closely adherent to each other by their sides, and provided with a moderate-sized, oval nucleus with one or two nucleoli. The length of the cells is from $\frac{1}{800}$ to $\frac{1}{500}$ of an inch, and their diameter from $\frac{1}{3000}$ to $\frac{1}{2500}$ of an inch. When villosities exist on the surface of the membranes, the cells follow the elevations and do not fill up the spaces between them, as in most of the membranes covered with pavement-epithelium.

The mucous membrane of the urinary bladder, the ureters, and the pelvis of the kidneys, cannot be classed in either of the above divisions. They are covered with mixed epithelium, presenting all varieties of form between the pavement and the columnar, some of the cells being caudate and quite irregular.

Mechanism of the Secretion of Mucus.—Nearly every one of the great variety of fluids known under the name of mucus is composed of the products of several different glandular structures. According to Robin, mucus proper is produced by the epithelial cells of that portion of the membrane situated on the surface, between the opening of the so-called mucous follicles or glands;[1] while the secretion of these special glandular organs always possesses peculiar properties. It is undoubtedly true that certain membranes which do not possess glands, as the mucous lining of the ureters and a great portion of the urinary bladder, are capable of secreting

of the air-passages; and vol. ii., Digestion, pp. 212, 313, and 389, for a description of the glands of the stomach and intestines.

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 438.

mucus. The mucous membrane of the stomach produces an alkaline, viscid secretion, during the intervals of digestion, when the gastric tubules do not act; and the gastric tubules, during digestion, secrete a fluid of an entirely different character. The fluid produced by the follicles of the small intestine likewise has peculiar digestive properties. These circumstances, and the fact that the entire extent of the mucous membranes is covered with more or less secretion, show that the general epithelial covering of these membranes is capable of secreting a fluid which forms one of the constituents of what is ordinarily recognized as mucus. It is impossible, however, to separate the secretion of the superficial layer of cells from the other fluids that are found on the mucous membranes; and it will be more convenient to regard as mucus, the secretion which is found upon mucous membranes, except when, as in the case of the gastric or the intestinal juice, we can recognize a special fluid by certain distinctive physiological properties.

In the membranes covered with cylinder-epithelium, which are usually provided with numerous simple follicles, the secretion is produced mainly by these follicles, but in part by the epithelium covering the general surface. The membranes covered with pavement-epithelium usually contain but few follicles, and are provided with simple racemose glands situated in the submucous structure, which are to be regarded rather as appendages to the membrane. The secretion is here produced by the epithelium on the free surface, and is always mixed with fluids resulting from the action of the mucous glands.

There is nothing to be said with regard to the mechanism of the secretion of mucus beyond what has already been stated in connection with the general mechanism of secretion. All the mucous membranes are quite vascular, and the cells covering the membrane and lining the follicles and glands attached to it have the property of taking from the blood the materials necessary for the formation of the secretion

These principles pass out of the cells upon the surface of the membrane in connection with water and inorganic salts in variable proportion. Many of the cells themselves are desquamated, and are found in the secretion, together with a few leucocytes, which are produced upon mucous surfaces with great facility.

Composition and Varieties of Mucus.—In comparing the secretions of the different mucous membranes, each one will be found to possess certain distinctive peculiarities, more or less marked; but there are certain general characters which belong to all varieties of mucus. The fluid is usually a mixture of the secretion from the simple membrane and the product of its follicles or glandular appendages, and always contains a certain amount of desquamated epithelium; and it is frequently possible, from the microscopical characters of the epithelium, to indicate the part by which any given specimen of mucus was secreted. This desquamation of epithelium must not be regarded as a necessary condition of the secretion of mucus, any more than the desquamation of the epidermic scales is to be regarded as a condition necessary to the secretion of perspiration or sebaceous matter. It is a property of the epidermis and the epithelial covering of mucous membranes to be regenerated by the formation of new cells from below, the effete structures being thrown off, and the admixture of these with mucus is simply accidental. The leucocytes, formerly called mucus-corpuscles, are the result of irritation of the mucous membrane, and are not constant constituents of normal mucus.

All the varieties of mucus are more or less viscid; but this character is very variable in the secretions from different membranes, in some of them the secretion being quite fluid, and in others almost semisolid.

The different kinds of mucus vary considerably in general appearance. Some of them are perfectly clear and colorless; but the secretion is generally grayish and semitransparent.

Examined by the microscope, in addition to the mixture of epithelium and occasional leucocytes, which give to the fluid its semiopaque character, the mass of the secretion presents a very finely striated appearance, as though it were composed of thin layers of a nearly transparent substance, with many folds. These delicate striæ do not usually interlace with each other, and are rendered more distinct by the action of acetic acid. This appearance, with the peculiar effect of the acid, is characteristic of mucus. Some varieties of mucus present very fine, pale granulations and a few small globules of oil.

On the addition of water, mucus is somewhat swollen, but is not dissolved. An exception to this is the secretion of the conjunctival mucous membrane, which is coagulated on the addition of water.

As a rule, the reaction of mucus is alkaline; the only exception to this being the vaginal mucus, which is very fluid and distinctly acid.

It is exceedingly difficult to get an exact idea of the proximate composition of normal mucus, from the fact that the quantity secreted by the membranes in their natural condition is very small, being just sufficient to lubricate their surface. All varieties, however, contain a peculiar organic principle, called mucosine, which gives the fluid its peculiar viscidity They likewise present a considerable variety of inorganic salts; as the chlorides of sodium and potassium, alkaline lactates, carbonate of soda, phosphate of lime, a small proportion of the sulphates, and, in some varieties, traces of iron and silica.[1]

Of all these constituents, mucosine is the most important, as it gives to the secretion its characteristic properties. Like all other organic nitrogenized principles, mucosine is coagulable by various reagents. It is imperfectly coagulated by heat; and after desiccation can be made to assume its peculiar con-

[1] SIMON, *Animal Chemistry with reference to the Physiology and Pathology of Man*, Philadelphia, 1846, p. 351.

sistence by the addition of a small quantity of water. It is coagulated by acetic acid and by a small quantity of the strong mineral acids, being redissolved in an excess of the latter. It is also coagulated by strong alcohol, forming a fibrinous clot soluble in hot and cold water. Mucosine may be readily isolated by adding water to a specimen of normal mucus, filtering, and precipitating with an excess of alcohol. If this precipitate, after having been dried, be exposed to water, it assumes the viscid consistence peculiar to mucosine. This property serves to distinguish it from albumen and other organic nitrogenized principles.

Nasal Mucus.—The nasal mucus, being subject to so many changes from irritation of the Schneiderian membrane, presents considerable variation in its appearance and composition. Under perfectly normal conditions, it is very viscid, clear or slightly opaque and grayish, and strongly alkaline. It always contains more or less columnar epithelium. In its behavior to various reagents, it presents the characteristics which we have ascribed to the secretions of the mucous membranes generally. The following is the composition of the normal secretion:

Composition of Nasal Mucus.[1]

Water	933·00	to	947·00
Mucosine (with a trace of albumen?)	53·30	"	54·80
Lactate of soda (?)	1·00	"	5·00
Organic crystalline principles	2·00	"	1·05
Fatty matters and cholesterine	not estimated		5·01
Chlorides of sodium and potassium	5·60	to	5·09
Calcareous and alkaline phosphates	3·50	"	2·00
Sulphate and carbonate of soda	0·90	not estimated.	

Bronchial and Pulmonary Mucus.—This is the secretion of the general mucous surface of the larynx and bronchial tubes, mixed with the products of the glands situated in the substance of these membranes and in the submucous

[1] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 450.

tissue. In addition to this secretion, there is an exhalation of watery vapor containing traces of organic matter, coming from the air-cells and the bronchial tubes less than $\frac{1}{50}$ of an inch in diameter, which are not provided with mucous glands. This variety of mucus is alkaline and is quite similar to nasal mucus in its appearance and general characters. The following is an analysis, by Nasse, of the secretion expectorated in the morning by a healthy man:

Composition of Bronchial and Pulmonary Mucus.[1]

Water	955·520
Mucosine, with a little albumen	23·754
Watery extract	8·006
Alcoholic extract	1·810
Fat	2·887
Chloride of sodium	5·825
Sulphate of soda	0·400
Carbonate of soda	0·198
Phosphate of soda	0·080
Phosphate of lime, with traces of iron	0·974
Carbonate of lime	0·291
Silica and sulphate of lime	0·255
	1,000·000

Mucus secreted by the Mucous Membrane of the Alimentary Canal.—Throughout the alimentary canal, from the mouth to the anus, the lining membrane secretes a certain quantity of mucus, which does not differ very much from the mucus found in other situations. This secretion appears to take place independently of the act of digestion, and the mucus in most parts of the tract is not known to possess any peculiar digestive properties. By ligating all of the salivary ducts, the buccal mucus has been procured. This secretion is produced by the cells covering the general surface of the membrane, and is mixed with the secretion of the isolated follicular and racemose glands of the mouth. An ana-

[1] Nasse, *Ueber die Bestandtheile des normalen Schleims der Luftwege.—Journal für praktische Chemie*, Leipzig, 1843, Bd. xxix., S. 65.

ogous secretion is produced by the mucous membrane of the pharynx and œsophagus.[1] During the intervals of digestion, a viscid, alkaline secretion covers the mucous membrane of the stomach. The digestive secretions of the small intestine are so viscid that it has been found impossible to separate them from the true mucous secretion; but undoubtedly a secretion of ordinary mucus is constantly taking place from the lining membrane of both the small and the large intestine. This secretion probably has a purely mechanical function, serving to lubricate the membranes and facilitate the movements of the opposing surfaces against each other.

The mucous membrane of the gall-bladder produces quite an abundant secretion; but this is always mixed with the bile, and will be considered in connection with the composition of this fluid, though it is not known to possess any peculiar properties.

Mucus of the Urinary Passages.—A small quantity of mucus is secreted by the urinary passages. This is present in the normal urine, in the form of a very slight, cloudy deposit, which forms after the urine has been allowed to stand for a few hours. A certain amount of secretion takes place from the mucous membrane of the bladder, which, as we have seen, does not possess glands except near the neck. This secretion takes place in very small quantity, and may be recognized in the urine by the ordinary microscopical characters of mucus.

Mucus of the Generative Passages.—The vagina secretes a small quantity of mucus, which differs from the secretions of the other mucous membranes in being distinctly acid and almost entirely wanting in viscidity. The mucus of the neck of the uterus is clear, viscid, and distinctly alkaline. This is ordinarily produced in small quantity, but is very

[1] See vol. ii., Digestion, p. 166.

abundant during pregnancy. It is the result of the action chiefly of the large, rounded glands found in this situation. The mucus of the body of the uterus and of the Fallopian tubes is alkaline, of a grayish color, and slightly viscid. The secretions of these parts are greatly modified during menstruation. These considerations, however, belong properly to the subject of generation, and will be taken up more fully in another volume.

Conjunctival Mucus.—A small quantity of a viscid secretion constantly covers the conjunctival mucous membrane, and is a mixture of the secretion of the membrane itself with the fluid produced by the little mucous glands found near the internal angle of the eye. A peculiarity of this variety of mucus, mentioned by Robin, is that it becomes white, like coagulated albumen, by the action of pure water.[1]

A peculiarity of the mucus from the conjunctiva, the urethra of the male, and the vagina, is that they readily become virulent when secreted in abnormal quantity. They then contain a large number of leucocytes, and have a more or less puriform character; but the virulent principle is contained in the clear liquid.

General Function of Mucus.—The smooth, viscid, and adhesive character of mucus, forming, as this fluid does, a coating for the mucous membranes, serves to protect these parts, enables their surfaces to move freely one upon the other, and modifies to a certain extent the process of absorption. This function is entirely independent of the function of some of the mucous glands, as the follicles of Lieberkühn, which produce secretions only at particular times.

Aside from the mechanical functions of mucus, it has been shown that this fluid, in connection with the epithelial covering of the mucous membranes, is capable of preventing the absorption of certain principles. It is well known, for

[1] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 447.

example, that venoms may be applied with impunity to certain mucous surfaces, while they produce poisonous effects if introduced into the circulation. These agents are not neutralized by the secretions of the parts, for they will produce their characteristic effects upon the system when removed from the mucous surfaces and introduced into the circulation; and it is reasonable to suppose that the mucous membranes are capable of resisting their absorption. This fact is proven by the following interesting experiment detailed by Robin:

Let an endosmometer be constructed, using a fresh mucous membrane, on the surface of which the epithelium and layer of mucus remain intact, and in the interior of the apparatus, place a saccharine solution, and let the membrane be exposed to a solution containing some venomous fluid. The liquid will mount in the interior of the apparatus, but the poison will not penetrate the membrane. If the mucus and epithelium be now removed with the finger-nail from even a small portion of the membrane, the poison will immediately pass through that part of the membrane, and an animal may be killed with the fluid which now penetrates into the interior of the endosmometer.[1]

These facts show that mucus is an important secretion. It not only has a useful mechanical function, but it is in all probability closely connected with some of the phenomena of elective absorption which are so often observed, particularly in the alimentary canal.

Sebaceous Fluids.

The general cutaneous surface is constantly lubricated by a small quantity of a peculiar oily secretion, called sebum, or sebaceous matter. This secretion is somewhat modified in certain situations, and an analogous fluid is produced by glands of a peculiar structure opening into the

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 439.

external meatus of the ear. Another fluid, very much like the ordinary sebaceous matter, is smeared upon the edges of the eyelids. These secretions, called respectively cerumen and Meibomian fluid, resemble the secretion of the ordinary sebaceous glands sufficiently to be classed with it.

Physiological Anatomy of the Sebaceous, Ceruminous, and Meibomian Glands.—The true sebaceous glands are found in all parts of the body that are provided with hair; and as nearly every part of the general surface presents either the long, the short, or the downy hairs, these glands are very generally distributed. They exist, indeed, in greater or less numbers in all parts of the skin, except the palms of the hands and the soles of the feet. In the labia minora in the female, and in portions of the prepuce and glans penis of the male, parts not provided with hair, small racemose sebaceous glands are found, which produce secretions differing somewhat from that formed by the ordinary glands. The glands in the areola of the nipple in the female are very large, and are connected with small, downy hairs. Kölliker has observed these glands, not connected with hairs, upon the nipple of the male.[1]

Nearly all of the sebaceous glands are either simple racemose glands, that is, presenting a number of follicles connected with a single excretory duct, or compound racemose glands, presenting several ducts, with their follicles, opening by a common tube. Although there is this difference in the size and arrangement of the glands of the general surface, they secrete essentially the same fluid, and their anatomical differences consist simply in a multiplication of follicles.

The differences in the size of the sebaceous glands bear a certain relation to the size of the hairs with which they are connected; and, as a rule, the largest glands are connected with the small, downy hairs. These distinctions in size are

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 171.

so marked, that the glands may be divided into two classes; viz., those connected with the long hairs of the head, face, chest, axilla, and genital organs, and the coarse, short hairs, and those connected with the fine, downy hairs. A few small simple follicles are found in the parts not provided with hairs.[1]

The glands connected with the larger hair-follicles are of the simple racemose variety, and are from $\frac{1}{120}$ to $\frac{1}{40}$ of an inch in diameter. From two to five of these glands are generally found arranged around the follicle. They discharge their secretion at about the junction of the upper third with the lower two-thirds of the hair-follicle.[2] The follicles of the long hairs of the scalp are generally provided each with a pair of sebaceous glands, measuring from $\frac{1}{120}$ to $\frac{1}{75}$ of an inch in diameter. Encircling the hairs of the beard, the chest, axilla, and genital organs, are large glands, some of them $\frac{1}{40}$ of an inch in diameter, arranged in groups of from four to eight.

The glands connected with the follicles of the small, downy hairs, are so large, compared with the hair-follicles, that the latter seem rather as appendages to the glandular structure. These glands are of the compound racemose variety, and present sometimes as many as fifteen *culs-de-sac*. The largest are found on the nose, the ear, the caruncula lachrymalis, the penis, and the areola of the nipple, where they measure from $\frac{1}{50}$ to $\frac{1}{12}$ of an inch. The glands connected with the downy hairs of other parts are usually smaller. The glands of Tyson, situated upon the corona of the glans penis and behind, upon the cervix, are sebaceous glands of the compound racemose variety.[3]

The minute structure of the sebaceous glands is very

[1] Kölliker, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 146.

[2] See Fig. 5, page 125.

[3] A very full and satisfactory account of the distribution and general anatomy of the sebaceous glands is to be found in Kölliker, *Manual of Human Microscopic Anatomy*, London, 1860, p. 135, *et seq.*, and in the later German edition, Leipzig, 1867, S. 146, *et seq.*

simple. The follicles which compose the simple glands, and the follicular terminations of the simple and compound racemose glands, are formed of a delicate, structureless or slightly granular membrane, with an external layer of inelastic and small elastic fibres, and are lined by cells. Next the membrane the cells are polyhedric, pale, and granular, most of them presenting a nucleus and nucleolus; but the follicle itself contains fatty granules and the other constituents of the sebaceous matter, with cells filled with fatty particles. These cells abound in the sebaceous matter as it is discharged from the duct. The great quantity of fatty granules and globules found in the ducts and follicles of the sebaceous glands renders them dark and opaque when examined with the microscope by transmitted light, and their appearance is quite distinctive. The larger glands are surrounded with capillary blood-vessels.

FIG. 1.

A very large sebaceous gland from the nose, with a small hair-follicle opening into it. Magnified fifty diameters. (KÖLLIKER, *Handbuch der Gewebelehre*, Leipzig, 1867, S. 147.)

The ceruminous glands of the ear produce a secretion resembling the sebaceous matter in many regards, but in their anatomy they are almost identical with the sudoriparous glands. They belong to the variety of glands called tubular, and consist of a nearly straight tube which penetrates the skin, and a rounded or ovoid coil situated in the subcutaneous structure. These glands are found only in the cartilaginous portion of the external meatus, where they exist in great numbers. They are rather more numerous in the inner than in the outer half of the meatus.

The ducts are short and nearly straight, simply penetrating the different layers of the skin, and are from $\frac{1}{700}$ to $\frac{1}{500}$ of an inch in diameter. Their openings are rounded and about $\frac{1}{250}$ of an inch in diameter. They sometimes terminate in the upper part of one of the hair follicles. They present an external coat of white fibrous tissue, and are lined with several layers of small, pale, nucleated epithelial cells.

FIG. 2.

Vertical section of the skin of the external auditory meatus. 1, 1, Epidermis; 2, 2, Derma; 3, 3, Series of hair-follicles lodged in the substance of the skin; 4, 4, Series of sebaceous glands attached to these follicles; 5, 5, Subcutaneous areolar layer; 6, 6, Ceruminous glands; 7, 7, Ceruminous glands with the ducts divided; 8, 8, Adipose vesicles. (SAPPEY, *Traité d'anatomie*, Paris, 1852, tome ii., p. 523.)

The glandular coil is an ovoid or rounded, brownish mass, of from $\frac{1}{120}$ to $\frac{1}{50}$ or $\frac{1}{16}$ of an inch in diameter. It is simply a convoluted tube, continuous with the excretory duct and terminating in a somewhat dilated, rounded extremity. It presents occasionally, small, lateral protrusions. The diameter of the tube is from $\frac{1}{300}$ to $\frac{1}{250}$ of an inch. It possesses a fibrous coat with a longitudinal layer of invol-

untary muscular fibres, and externally a few elastic fibres It is lined by a single layer of irregularly-polygonal cells, from $\frac{1}{2000}$ to $\frac{1}{1200}$ of an inch in diameter. These cells contain numerous brownish or yellowish pigmentary granules. The tube forming the gland contains a clear fluid mixed with a granular substance containing cells.[1]

In addition to the ceruminous glands of the ear, numerous sebaceous follicles are found connected with the hair-follicles here, as in other parts provided with hair. The arrangement of the ordinary sebaceous glands and the ceruminous glands, which are situated in different planes in the subcutaneous structure, is shown in Fig. 2.

The Meibomian glands of the eyelids have essentially the same structure as the ordinary sebaceous glands. Their ducts, however, are longer, and the terminal follicles are arranged in a peculiar manner by the sides of the tubes, along their entire length.

These glands are situated partly in the substance of the tarsal cartilages, between their posterior surfaces and the conjunctival mucous membrane. They are placed at right angles to the free border of the eyelids, opening upon the inner edge, and occupying the entire width of the cartilages. From twenty-five to thirty glands are found in the upper, and from twenty to twenty-five in the lower lid.

Each gland consists of a nearly straight excretory duct, from $\frac{1}{300}$ to $\frac{1}{240}$ of an inch in diameter, communicating laterally with numerous compound racemose acini, or collections of follicles, measuring from $\frac{1}{300}$ to $\frac{1}{120}$ of an inch. From fifteen to twenty of these collections of follicles are found on either side of the duct in glands of medium length.[2] Most of the excretory ducts are nearly straight, but some are turned upon themselves near their upper extremity. The general arrangement of these glands is shown in Fig. 3.

[1] The measurements of these tubes and cells are taken from Kölliker (*op. cit.*, 1860, p. 133).

[2] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1852, tome ii., p. 598.

In general structure there is little, if any, difference between the terminal follicles of the Meibomian glands and the follicles of the ordinary sebaceous glands. They are lined with cells measuring from $\frac{1}{2400}$ to $\frac{1}{1200}$ of an inch in diameter. These cells contain numerous fatty globules, but they do not coalesce into large drops, such as are often seen in the ordinary sebaceous cells.[1] The follicles and ducts are filled with the whitish, oleaginous matter which constitutes the Meibomian secretion, or the sebum palpebrale.

FIG. 3.

Meibomian glands of the upper lid, magnified seven diameters. 1, 1. Free border of the lid; 2, 2. Anterior lip penetrated by the eyelashes; 3, 3. Posterior lip, with the openings of the Meibomian glands; 4, A gland passing obliquely at the summit; 5, Another gland bent upon itself; 6, 6, Two glands in the form of racemose glands at their origin; 7, A very small gland; 8, A medium-sized gland. (SAPPEY, *Traité d'anatomie*, Paris, 1852, tome ii., p. 597.)

In addition to the Meibomian secretion, the edges of the palpebral orifice receive a small amount of secretion from ordinary sebaceous glands of the compound racemose variety (ciliary glands), which are appended in pairs to each of the follicles of the eyelashes, and the sebaceous glands attached to the small hairs of the caruncula lachrymalis.

Ordinary Sebaceous Matter.—Although it may be inferred, from the great number of sebaceous glands opening

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 678.

upon the cutaneous surface, that the amount of sebaceous matter must be considerable, it has been impossible to collect the normal fluid in quantity sufficient for ultimate analysis. In certain parts, as the skin of the nose, where the glands are particularly abundant, a certain amount of oily secretion is sometimes observed, giving to the surface a greasy, glistening aspect. This may be absorbed by paper, giving it the well-known appearance produced by oily matters, and may be collected in small quantity upon a glass slide and examined microscopically. It then presents a number of strongly-refracting fatty globules, with a few epithelial cells. The cells, however, are not numerous in the fluid as it is discharged upon the general surface; but if the contents of the ducts and follicles be examined, cells will here be found in great abundance. Most of the cells, indeed, remain in the glands, and the oily matter only is discharged. The object of this secretion is to lubricate the general cutaneous surface, and to give to the hairs that softness which is characteristic of them when in a perfectly healthy condition.

It is only when the action of the sebaceous glands has become more or less modified, that the secretion can be obtained in sufficient quantity for chemical analysis; but we cannot be certain that the fluid taken under these conditions is perfectly normal. The analysis by Esenbeck,[1] which is often quoted in works on physiology, was the result of an examination of the contents of a largely-distended hair-follicle; and as the secretion was confined for a long time, it is evident that it must have undergone material alteration. We cannot, indeed, refer to any ultimate analysis of the normal sebaceous secretion; but of all the examinations that have been made of the secretion when it has been

[1] ESENBECK, *Chemische Untersuchung des Inhalts einer vergrösserten Talgdrüse der Haut (glandula sebacea) oder einer sogenannten Fettbalg-Geschwulst (Atheroma)*.—KASTNER'S *Archiv für die gesammete Naturlehre*, Nürnberg, 1827, B. xii., S. 460, *et seq.*)

considerably increased in quantity, those of Lutz give the best idea of what may be supposed to be nearly its ordinary composition. This observer analyzed the secretion in a case of general hypertrophy of the sebaceous system. The fluid which he extracted from the dilated glands was milky-white, and of about the consistence, when cold, of wax. The mean of eight analyses of this fluid was as follows:[1]

Composition of Sebaceous Matter.

Water	357
Oleine	270
Margarine	135
Butyric acid and butyrate of soda	3
Caseine	129
Albumen	2
Gelatine	87
Phosphate of soda and traces of phosphate of lime	7
Chloride of sodium	5
Sulphate of soda	5
	1,000

This analysis gives the proportions of animal and solid matters, desiccated in a current of dry air. Robin, who has reviewed at considerable length the analytical process employed by Lutz, regards the matter supposed to be either caseine or some analogous albuminoid substance, as the organic matter of the epithelial cells that exist in such great numbers in distended sebaceous glands. He regards the weight of the substances designated under the names of albumen, caseine, and gelatine, with a certain quantity of the water driven off by desiccation, as representing the proportion of epithelium.[2] This view is very reasonable, as the microscope always shows in these collections great numbers

[1] LUTZ, *De l'hypertrophie générale du système sébacé*—Thèse, No. 65, Paris, 1860, p. 18. The proportions of oleine and margarine are given on p. 20.

[2] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 599.

of epithelial cells. Cholesterine, which is present so frequently in the contents of sebaceous cysts, does not exist in the normal secretion, nor was it found in the analyses by Lutz.

During the latter periods of pregnancy and during lactation, the sebaceous glands of the areola of the nipple become considerably distended with a grayish-white, opaque secretion, containing numerous oily globules and granules. Frequently the fluid contains also a large number of epithelial cells. During the periods above indicated, the secretion here is always much more abundant than in the ordinary sebaceous glands.

Smegma of the Prepuce and of the Labia Minora.—In the folds of the prepuce of the male and the inner surface and folds of the labia minora in the female, a small quantity of a whitish, grumous matter, of a cheesy consistence, is sometimes found, particularly when proper attention is not paid to cleanliness. The matter which thus collects in the folds of the prepuce has really little analogy with the ordinary sebaceous secretion. Examination with the microscope shows that it is composed almost entirely of irregular scales of pavement-epithelium, which do not present the fatty granules and globules usually observed in the cells derived from the sebaceous glands. Robin regards the production of this substance as entirely independent of the secretion of sebaceous matter, as it is formed chiefly in parts of the prepuce in which the sebaceous glands are wanting.[1]

The smegma of the labia minora is of the same character as the smegma preputiale; but it contains drops of oil, and the other products of the sebaceous glands found in these parts.

Vernix Caseosa.—The surface of the fœtus at birth and

[1] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 587.

near the end of gestation is generally covered with a whitish coating, or smegma, called the vernix caseosa. This is most abundant in the folds of the skin; but it usually covers the entire surface with a coating of greater or less thickness and of about the consistence of lard. There are great differences in fœtuses at term, as regards the quantity of the vernix caseosa. In some the coating is so slight that it would not be observed unless on close inspection.

There are few analyses giving an accurate view of the ultimate composition of this substance;[1] and we can form the best idea of its constitution and mode of formation from microscopical examination. If a small quantity be scraped from the surface and be spread out upon a glass slide with a little glycerine and water, it will be found, on microscopical examination, to consist of an immense number of epithelial cells, with a very few small fatty granules. In the table given below it will be seen that these cells, after desiccation, constituted about ten per cent. of the whole mass. The fatty granulations are very few, and do not seem to be necessary constituents of the vernix, as they are of the sebaceous matter. In fact, the vernix caseosa must be regarded as the residue of the secretion of the sebaceous glands, rather than an accumulation of true sebaceous matter.

[1] The following table gives an approximative idea of the nature and quantity of the various substances that have been found in the vernix caseosa. This table was arranged by Robin from analyses by different observers:

Composition of the Vernix Caseosa.

Water	769·80 to 778·70
Nitrogenised matter, mucous or caseous	4·50
Desiccated epithelium	101·30
Cholesterine, Oleine and margarine, Oleates and margarates of potassa and of soda,	108·25
Chloride of sodium, Hydrochlorate of ammonia, Phosphate of soda and of lime, Ammonio-magnesian phosphate,	14·95

—Robin, *Leçons sur les humeurs*, Paris, 1867 p. 590.

The microscopical examination of the vernix caseosa is interesting from an anatomical point of view, and possesses considerable importance in certain medico-legal questions. The cells are polyhedric in form, somewhat flattened from mutual compression, and have a diameter of from $\frac{1}{1200}$ to $\frac{1}{800}$ of an inch. Their angles are irregular and rounded, not possessing that sharpness of definition which characterizes the epidermic cells of the fœtus. They are colorless, transparent, very often folded upon themselves, and have no nuclei. The cells themselves are very slightly granular, but a few dark fatty granules sometimes adhere to their exterior. These cells have no analogy with the ordinary epidermic cells, but resemble rather the cells found in sebaceous collections. They are regarded, therefore, by Robin, as derived entirely from the sebaceous glands.[1] The secretion of these glands is discharged upon the surface, and disappears in great part, leaving a residue of altered epithelial cells. It is on account of the absence, to a great degree, of oily matter, that the vernix caseosa is not softened by gentle heat.

The function of the vernix caseosa is undoubtedly protective. If we attempt to make a microscopical preparation of the cells with water, it becomes evident that the coating is penetrated by the liquid with very great difficulty, even when mixed with it as thoroughly as possible. Indeed, we never observe at birth the peculiar effects of prolonged contact of the cutaneous surface with water. The protecting coating of vernix caseosa allows the skin to perform its functions in utero, and at birth, when this coating is removed, the surface is found in a condition perfectly adapted to extra-uterine existence. It is not probable that the vernix

[1] Robin et Tardieu, *Mémoire sur l'examin microscopique des taches formées par le méconium et l'enduit fœtal, pour servir à l'histoire médico-légale de l'infanticide ; extrait des Annales d'hygiène publique et de médecine légale*, Paris, 1857, 2e série, tome vii.

caseosa is necessary to facilitate the passage of the child into the world, for the parts of the mother are always sufficiently lubricated with mucous secretion.

Cerumen.—A peculiar substance of a waxy consistence is secreted by the glands that have been described, in the external meatus, under the name of ceruminous glands, mixed with the secretion of sebaceous glands connected with the short hairs in this situation. It is difficult to ascertain what share these two sets of glands have in the formation of the cerumen. Robin is of the opinion that the waxy portion of the secretion is produced entirely by the sebaceous glands, and that the convoluted glands, commonly known as the ceruminous glands, produce a secretion like the perspiration. He calls the latter, indeed, the sudoriparous glands of the meatus.[1] This view is, to a certain extent, reasonable; for the sebaceous matter is not removed from the meatus by friction, as in other situations, and would have a natural tendency to accumulate. But the contents of the ducts of the ceruminous glands differ materially from the fluid found in the ducts of the ordinary sudoriparous glands, containing granules and fatty globules, such as exist in the cerumen. Although the glands of the ear are analogous in their structure, and, to a certain extent, in their secretion, to the perspiratory glands, the fluid which they produce is peculiar. We shall see, also, that the perspiratory glands of the axilla and of some other parts produce secretions differing somewhat from ordinary perspiration. As far as can be ascertained, the cerumen is produced by both sets of glands. The sebaceous glands attached to the hair-follicles probably secrete most of the oleaginous and waxy matter, while the so-called ceruminous glands produce a secretion of much greater fluidity, but containing a certain amount of granular and fatty matter.

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 591.

The consistence and general appearance of cerumen are quite variable within the limits of health. When first secreted, it is of a yellowish color, about the consistence of honey, becoming darker and much more viscid upon exposure to the air. It has a very decided and bitter taste. It readily forms a sort of emulsive mixture with water.

Examined microscopically, the cerumen is found to contain semisolid, dark granulations of an irregularly-polyhedric shape, epithelium from the sebaceous glands, and epidermic scales, both isolated and in layers. Sometimes also a few crystals of cholesterine are found.

Chemical examination shows that the cerumen is composed of oily matters fusible at a low temperature, a peculiar organic matter resembling mucosine, with salts of soda, and a certain quantity of phosphate of lime. The yellow coloring matter is soluble in alcohol; and the residue after evaporation of the alcohol is very soluble in water, and may be precipitated from its watery solution by the neutral acetate of lead or the chloride of tin. This extract has an exceedingly bitter taste.

The cerumen lubricates the external meatus, accumulating in the canal around the hairs. Its peculiar bitter taste is supposed to be efficient in preventing the entrance of insects.

Meibomian Secretion.—Very little is known concerning any special properties of the Meibomian fluid, except that it mixes with water in the form of an emulsion more readily than the other sebaceous secretions.[1] It is produced in small quantity, mixed with a certain amount of mucus and the secretion from the ordinary sebaceous glands attached to the eyelashes (ciliary glands), and the glands of the caruncula lachrymalis, and smears the edges of the palpebral

[1] ROBIN, *op. cit.*, p. 592.

orifice. This oily coating on the edges of the lids, unless the tears be produced in excessive quantity, prevents their overflow upon the cheeks, and directs the excess of fluid into the nasal duct.

CHAPTER III.

MAMMARY SECRETION.

Physiological anatomy of the mammary glands—Condition of the mammary glands during the intervals of lactation—Structure of the mammary glands during lactation—Mechanism of the secretion of milk—Conditions which modify the lacteal secretion—Influence of diet—Influence of liquid ingesta—Influence of alcoholic beverages—Influence of mental emotions—Quantity of milk—Properties and composition of milk—Specific gravity of milk—Coagulation of milk—Microscopical characters of milk—Composition of milk—Nitrogenized constituents of milk—Non-nitrogenized constituents of milk—Inorganic constituents of milk—Variations in the composition of milk—Colostrum—Composition of colostrum—Lacteal secretion in the newly-born—Composition of the milk of the infant.

The mammary glands are among the most remarkable organs in the economy; not only from the peculiar character of their secretion, which is unlike the product of any other of the glands, but from the great changes which they undergo at different periods, both in size and structure. Rudimentary in early life, and in the male at all periods of life, these organs are fully developed in the adult female, only in the latter months of pregnancy and during lactation. It is true, that in the female, after puberty, the mammary glands undergo a marked and rapid increase in size; but even then they are not fully developed, and if examined with the microscope, will be found to lack the essential anatomical characters of secreting organs. The physiological anatomy of the mammary glands consequently possesses

peculiar interest, aside from the great importance of their secretion.

It will be found convenient to consider these organs in three stages of development; viz., in their rudimentary condition, as they exist in the male and in the female before puberty; in the partially-developed state, as they are found in the unimpregnated female after puberty and during the intervals of lactation; and finally, in the fully-developed condition, when milk is secreted.

Physiological Anatomy of the Mammary Glands.

The form, size, and situation of the mammæ in the adult female are too well known to demand more than a passing mention. These organs are almost invariably double, and are situated on the anterior portion of the thorax over the great pectoral muscles. In women who have never borne children, they are generally firm, nearly hemispherical, with the nipple at the most prominent point. In women who have borne children, the glands, during the intervals of lactation, are usually larger, are held more loosely to the subjacent parts, and are apt to become flabby and pendulous. The areola of the nipple is also darker.

Certain rare examples are on record of anomalies in the number and location of the mammary glands. In some instances three, four, and five distinct glands have existed instead of two;[1] and some examples are related of extraordinary development of the mammary glands in the male, to such an extent as to afford sufficient nourishment for an infant.[2] A remarkable case of malposition of a mammary gland is reported by Dr. Robert, of Marseilles, in Magendie's

[1] Reference to a number of these cases is made by Dr. Solly, in the *Cyclopædia of Anatomy and Physiology*, London, 1839–1847, vol. iii., p. 251.

[2] Quite a number of cases of this kind are on record, many of them well authenticated. Dr. Dunglison gives a full account of several instances of lactation in the male, attested by competent medical observers. (DUNGLISON, *Human Physiology*, Philadelphia, 1856, vol. ii., p. 520.)

Journal of Physiology. In this case there was a well-formed mammary gland on the external surface of the left thigh, about four inches below the great trochanter. The mammary glands upon the chest performed their function with regularity, and were normal in all respects; but the gland upon the thigh secreted during lactation such a quantity of milk, that the woman had nourished all her children, seven in number, indifferently from the three glands. She had nursed one of her children in this way for thirty-three months. It is a remarkable fact, that the mother of this woman had three mammary glands, one on the left side of the chest and two on the right. This case is perfectly authentic, and was reported on by MM. Chaussier and Magendie, a committee from the French Academy of Sciences.[1]

In many works on physiology, instances of unusual lactation are quoted; but although the time and duration of the process are modified, the character of the secretion is not altered. A case is reported as occurring in this country, in which lactation continued in a woman sixty-five years of age.[2]

At birth, in both sexes, the mammary glands are nearly as fully developed as at any time before puberty. They make their appearance about the fourth month, in the form of little elevations of the structure of the true skin, which soon begin to send out processes destined to be developed into the lobes of the glands. At birth the glands measure hardly more than one-third of an inch in diameter. At this time there are from twelve to fifteen lobes in each gland, and every lobe is penetrated by a duct, with but few

[1] Chaussier et Magendie, *Rapport fait à l'Académie des Sciences sur une observation de M. le Dr. Robert, de Marseille, relative à une femme qui a allaité plusieurs enfans avec une mamelle située à la cuisse gauche.—Journal de physiologie*, Paris, 1827, tome vii., p. 175.

[2] Dunglison, *Human Physiology*, Philadelphia, 1856, vol. ii., p. 518. The reader is referred to the work of Dr. Dunglison for an account of a number of very curious instances of unusual lactation.

branches, composed of fibrous tissue and lined with columnar epithelium. The ends of these ducts are frequently somewhat dilated; but what have been called the gland-vesicles do not make their appearance before puberty. In the male the glands are from one half an inch to two inches broad, and from $\frac{1}{12}$ to $\frac{1}{4}$ of an inch in thickness. In their structure, however, they present little if any difference from the rudimentary glands of the infant.

As the period of puberty approaches in the female, the rudimentary ducts of the different lobes become more and more ramified. Instead of each duct having but two or three branches, the different lobes, as the gland enlarges, are penetrated by innumerable ramifications, which have gradually been developed as processes from the main duct. It is important to remember, however, that these branches are never so numerous or so long during the intervals of lactation as they are when the organ is in full activity. The ordinary condition of the gland, as compared with its structure during activity, is that of atrophy.

Condition of the Mammary Glands during the Intervals of Lactation.—At this time the gland is not a secreting organ. It presents the ducts, ramifying, to a certain extent, in the substance of the lobes into which the structure is divided, but their branches are short and possess but few of the glandular acini that are observed in every part of the organ during lactation. This difference in the structure of the gland is most remarkable; and as it passes from a secreting to a non-secreting condition at the end of lactation, the ducts retract in all their branches, and most of the secreting *culs-de-sac* disappear. At this time the glandular tissue is of a bluish-white color, and loses the granular appearance which it presents during activity. The ducts are then lined with a small, nucleated, pavement-epithelium, which is not found during the secretion of milk. These changes, pointed out by Robin, whose observations have

been verified and extended by Sappey,[1] are confined almost exclusively to the secreting structure of the gland. The interstitial tissue remains about the same, the blood-vessels, only, being increased in number during lactation. As we are treating of the mammary glands as secreting organs, a full description of its structure is deferred until we come to consider it in a state of functional activity.

Structure of the Mammary Glands during Lactation.—Between the fourth and the fifth month of utero-gestation, the mammary glands begin to increase in size; and at term, they are very much larger than during the unimpregnated state. At this time the breasts become quite hard; and the surface near the areola is somewhat uneven, from the great development of the ducts. The nipple itself is increased in size, the papillæ upon its surface and upon the areola are more largely developed, and the areola becomes larger, darker, and thicker. The glandular structure of the breasts during the latter half of pregnancy becomes so far developed, that if the child be born at the seventh month, the lacteal secretion may generally be established at the usual period after parturition. Even when parturition takes place at term, a few days elapse before secretion is fully established, and the first product of the gland, called colostrum, is very different from the fully-formed milk.

The only parts of the covering of the breasts that present any peculiarities are the areola and the nipple. The surface of the nipple is covered with papillæ, which are very largely developed near its summit. It is covered by epithelium in several layers, the lower strata being filled with pigmentary granules. The true skin covering the nipples is composed of inelastic and elastic fibres, containing a large number of sebaceous glands, but no hair-follicles nor sudoriparous glands. According to Sappey, these glands, which are from eighty to one hundred and fifty in number, are always of the racemose variety, and never exist in the form

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 697.

of simple follicles, as they are described by most anatomists.[1] The nipple contains the lactiferous ducts, fibres of inelastic and elastic tissue, with an immense number of non-striated muscular fibres. The muscular fibres have no definite direction, but are so numerous, that when they are contracted, the nipple becomes very firm and hard. The nipple, though it may thus become hard upon the application of cold or other stimulus, presents none of the anatomical characteristics of the true erectile organs, as is erroneously supposed by some authors; and its hardening is simply due to contraction of its muscular fibres.[2]

The areola does not lie, like the general integument covering the gland, upon a bed of adipose tissue, but is closely adherent to the subjacent glandular structures. The skin here is much thinner and more delicate than in other parts, and the pigmentary granules are very abundant in some of the lower strata of epidermic cells, particularly during pregnancy. The true skin of the areola is composed of inelastic and elastic fibres, and lies upon a distinct layer of non-striated muscular fibres. The arrangement of the muscular fibres (sometimes called the subareolar muscle) is quite regular, forming concentric rings around the nipple. These fibres are supposed to be useful in compressing the ducts during the discharge of milk. The areolar presents numerous papillæ, considerably smaller than those upon the nipple; hair-follicles, containing small, rudimentary hairs; sudoriparous glands; and sebaceous glands connected with the hair-follicles. The sebaceous glands in this situation are very large, and their situation is indicated by little prominences at the surface of the areola, which are especially marked during pregnancy.

The gland itself is of the compound racemose variety. It is covered in front by a subcutaneous layer of fat, and posteriorly is enveloped in a fibrous membrane loosely at-

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 594.

[2] For the anatomy of the erectile tissues, see vol. i., Circulation, p. 336.

tached to the pectoralis major. A considerable amount of adipose tissue is also found in the substance of the gland, between the lobes.

Separated from the adipose and fibrous tissue, the organ is found divided into lobes, from fifteen to twenty-four in number. These, in their turn, are subdivided into lobules made up of a greater or less number of acini or *culs-de-sac*. The secreting structure is of a reddish-yellow color, and is distinctly granular, presenting a decided contrast to the pale and uniformly-fibrous appearance of the gland during the intervals of lactation. If the ducts be injected from the nipple and be followed into the substance of the gland, each one will be found distributing its branches to a distinct lobe; so that the organ is really made up of a number of glands, in their structure identical with each other. It will be most convenient, in studying the intimate structure of the gland, to begin at the nipple and follow out one of the ducts to the termination of its branches in the secreting *culs-de-sac*.

The canals which discharge the milk at the nipple are called lactiferous, or galactophorous ducts. They vary in number from ten to fourteen. The openings of the ducts at the nipple are very small, measuring only from $\frac{1}{60}$ to $\frac{1}{40}$ of an inch. As each duct passes down, it enlarges in the nipple to $\frac{1}{25}$ or $\frac{1}{12}$ of an inch in diameter, and beneath the areola presents an elongated dilatation, from $\frac{1}{6}$ to $\frac{1}{3}$ of an inch in diameter, called the sinus of the duct.[1] During lactation a considerable quantity of milk collects in these sinuses, which serve as reservoirs. Beyond the sinuses the caliber of the ducts is from $\frac{1}{12}$ to $\frac{1}{6}$ of an inch. They penetrate the different lobes, branching and subdividing, to terminate finally in the collections of *culs-de-sac* which form the acini. Most modern observers are agreed that there is no anastomosis between the different lactiferous ducts, and that each one is distributed independently to one or more lobes.

[1] Kölliker, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 571

The intimate structure of the lactiferous ducts is interesting and important. They are possessed of three distinct coats. The external coat is composed of anastomosing fibres of elastic tissue, with some fibres of inelastic tissue. The middle coat is composed of non-striated muscular fibres, arranged longitudinally and existing throughout the duct, from its opening at the nipple to the secreting *culs-de-sac*. The internal coat is an amorphous membrane, lined with roundish or elongated cells during the intervals of lactation and even during pregnancy, but deprived of epithelium during the period when the lacteal secretion is most active.[1]

The acini of the gland, which are very numerous, are visible to the naked eye, in the form of small, rounded granules, of a reddish-yellow color. Between these acini there exist a certain quantity of the ordinary white fibrous tissue and quite a number of adipose vesicles. The presence of adipose tissue in considerable quantity in the substance of the glandular structure is peculiar to the mammary glands. Each acinus is made up of from twenty to forty secreting vesicles, or *culs-de-sac*. These vesicles are irregular in form, often varicose, and sometimes enlarged and imperfectly bifurcated at their terminal extremities. During lactation their diameter is from $\frac{1}{400}$ to $\frac{1}{300}$ of an inch. During pregnancy, and when the gland has just arrived at its full development, the secreting vesicles are formed of a structureless membrane, lined with small, nucleated cells of pavement-epithelium. The nuclei are relatively large, ovoid, and embedded in a small amount of amorphous matter, so that they almost touch each other. Sometimes the epithelium is segmented, and sometimes it exists in the form of a continuous nucleated sheet. When the secretion of milk becomes active, the epithelium entirely disappears, and reappears as the secretion diminishes. This observation is due to Robin,[2] and has an

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 697.

[2] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Mamelle*.

important bearing upon the mechanism of the secretion of milk.

During the intervals of lactation, as the lactiferous ducts become retracted, the glandular *culs-de-sac* disappear; and in pregnancy, as the gland takes on its full development, the ducts branch and extend themselves, and the vesicles are gradually developed around their terminal extremities. These changes in the development of the mammæ at different periods are most remarkable, and are not observed in any other part of the glandular system.[1]

FIG. 4.

Ducts and acini of the mammary gland. (LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865. Article, *Mamelle*.) *m*, nipple; *ss*, larger ducts; *r*, small duct; *u*, acini.

Mechanism of the Secretion of Milk.—With the exception of water and inorganic principles, all the important and characteristic constituents of the milk are formed in the substance of the mammary glands. The secreting structures have the property of separating from the blood a great variety of inorganic principles; and we shall see, when we come to study the composition of the milk more minutely, that it furnishes

[1] Sir Astley Cooper, in his admirable monograph upon the anatomy and diseases of the breast, published in 1840, was the first to give any clear idea of the minute structure of the mammary glands. His observations, however, have been much extended by later anatomists. The paper on the breast has been republished in this country. COOPER, *The Anatomy and Diseases of the Breast, with numerous plates. To which are added his various Surgical Papers, now first published in a collected form*, Philadelphia, 1845.

all the inorganic matter necessary for the nutrition of the infant, containing, even, a small quantity of iron. Precisely how the secreting vesicles separate the proper quantity of these principles from the circulating fluid, we are unable, in the present state of our knowledge, to determine. It is unsatisfactory enough to say that the membranes of the vesicles have an elective action, but this expresses the extent of our information on the subject.

The lactose, or sugar of milk, the caseine, and the fatty particles, are all produced, *de novo*, in the gland. The peculiar kind of sugar here found does not exist anywhere else in the organism. Even when the secretion of milk is most active, different varieties of sugar, such as glucose or cane-sugar, injected into the blood-vessels of a living animal, are never eliminated by the mammary glands, as they are by the kidneys; and their presence in the blood does not influence the quantity of lactose found in the milk. All that can be said with regard to the formation of sugar of milk is, that it is produced in the mammary glands. The mechanism of its formation is not understood.

Caseine is produced in the mammary glands, probably by a peculiar transformation of the albuminoid constituents of the blood. This principle does not exist in the blood, though its presence here has been indicated by some observers. The substance in the blood that has been mistaken for caseine is undoubtedly albumen, which will not respond to some of the tests on account of the alkalinity of the fluid in which it is contained. It is well known that the caseine of milk is precipitated by an excess of sulphate of magnesia; but the so-called caseine of the blood is not affected by this salt, and passes through it like albumen.[1]

The fatty particles of the milk are likewise produced in the substance of the gland, and the peculiar kind of fat which exists in this secretion is not found in the blood. The mechanism of the production of fat in the mammary

[1] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 283.

glands is obscure. The particles are not produced in cells and set free by their rupture, by a process analogous to that which takes place in the formation of the fatty particles found in the sebaceous matter, for during the time when the secretion of milk is most active, the epithelium of the secreting *culs-de-sac* has entirely disappeared. The butter is produced by the action of the amorphous walls of the vesicles, in the same way, probably, that fat is produced by the vesicles of the ordinary adipose tissue. At least, this is all that is known regarding the mechanism of its production.

As regards the mechanism of the formation of the peculiar and characteristic constituents of the milk, the mammary glands are to be classed among the organs of secretion, and not those of elimination or excretion; for none of these elements preëxist in the blood, but all appear first in the substance of the glands.

During the period of secretion, the glands receive a much larger supply of blood than at other times. Pregnancy favors the development of the secreting portions of the glands, but does not induce secretion. On the other hand, when pregnancy occurs during lactation, it diminishes, modifies, and may arrest the secretion of milk. The secretion is destined, however, for the nourishment of the child, and not for use in the economy of the mother—an important point of distinction from all other secretions—and its production presents one or two interesting peculiarities.

In the first place, the secreting action of the mammary glands is nearly continuous. When the secretion of milk has become fully established, while there may be certain periods when it is formed in greater quantity than at others, there is no absolute intermittency in its production.

Again, in all the other glandular organs, the epithelial cells found in their secreting portion seem to be the active agents in the production of the secretions; but in the mammary glands, as we have already noted, the epithelium

entirely disappears from the secreting *culs-de-sac* during the period of greatest functional activity of the gland, and nothing is left to perform the work of secretion but the amorphous membrane of the vesicles.

Conditions which modify the Lacteal Secretion.—Very little is known concerning the physiological conditions which modify the secretion of milk. When lactation is fully established, the quantity and quality of the milk secreted become adapted to the requirements of the child at different periods of its existence. In studying the composition of the milk, therefore, it will be found to vary considerably in the different stages of lactation. It is evident that, as the development of the child advances, a constant increase of nourishment is demanded; and, as a rule, the mother is capable of supplying all the nutritive requirements of the infant for from eight to twenty months.

During the time when such an amount of nutritive matter is furnished to the child, the quantity of food taken by the mother is sensibly increased; but observations have shown that the secretion of milk is not much influenced by the nature of the food. It is necessary that the mother should be supplied with good, nutritious articles; but as far as solid food is concerned, there seems to be no great difference between a coarse and a delicate alimentation; and the milk of females in the lower walks of life, when the general condition is normal, is fully as good as in women who are enabled to live luxuriously. It is, indeed, a fact generally recognized by physiologists, that the secretion of milk is little influenced by any special diet, provided the alimentation be sufficient and of the quality ordinarily required by the system, and that it contain none of the few articles of food which are known to have a special influence upon lactation. So long as the mother is healthy and well nourished, the milk will take care of itself; and the appetite is the surest guide to the proper variety, quality, and quantity of

food. It is very common, however, for females to become quite fat during lactation; which shows that the fatty elements of the food do not pass exclusively into the milk, but that there is a tendency, at the same time, to a deposition of adipose tissue in the ordinary situations in which it is found. It is a matter of common experience, that certain articles, such as acids and fermentible substances, often disturb the digestive organs of the child without producing any change in the milk, that can be recognized by chemical analysis. The individual differences in women, in this regard, are very great.

There are certain medicinal substances which are sometimes found to exert a powerful influence in diminishing or even arresting the secretion of milk, but a full consideration of these belongs to therapeutics. The same remark applies to the influence of electricity applied directly to the mammary glands.

The statements with regard to solid food do not apply to liquids. During lactation there is always an increased demand for water and liquids generally; and if these be not supplied in sufficient quantity, the secretion of milk is diminished, and its quality is almost always impaired. It is a curious fact, which has been fully established by observations upon the human subject and the inferior animals, that while the quantity of milk is increased by taking a large amount of simple water, the solid constituents are also increased, and the milk retains all of its qualities as a nutritive fluid. The late observations on this subject, by Dancel, illustrate very fully the unusual demand for liquids during lactation, and their influence upon the mammary secretion.[1]

Alcohol, especially when largely diluted, as in malt-liquors and other mild beverages, is well known to exert an influence upon the secretion of milk. Drinks of this kind

[1] DANCEL, *De l'influence de l'eau dans la production du lait.—Comptes rendus*, Paris, 1865, tome lxi., p. 243.

almost always temporarily increase the activity of the secretion, and sometimes produce a certain amount of effect upon the child; but direct and accurate observations on the actual passage of alcohol into the milk are wanting. During lactation the moderate use of drinks containing a small proportion of alcohol is frequently beneficial, particularly in assisting the mother to sustain the unusual drain upon the system. There are, however, few instances of normal lactation in which their use is absolutely necessary.

It has been conclusively shown that many medicinal articles administered to the mother pass unchanged into the mammary secretion, and therapeutists have sometimes attempted to produce the peculiar effects of certain remedies in this way in the child. This, however, can hardly be called a physiological action; but it is interesting to note that some articles may be eliminated in the milk, while others pass into other secretions. This elective power we have already seen is possessed by many of the glands. Among the articles that pass readily into the milk may be mentioned, some of the salts of soda, chloride of sodium, the sesquioxide of iron, and the preparations of iodine. Dr. Rees detected iodine in the milk in a patient who had taken but forty-five grains of the iodide of potassium in five-grain doses three times daily.[1] It is generally believed, from the effects upon the child of remedial agents administered to the mother, that very many articles of this class pass into the milk, but in such small quantity that they cannot be detected by the ordinary chemical tests.

It is well known that the secretion of milk may be profoundly affected by violent mental emotions. This is the case with many other secretions, as the saliva, and the gastric juice. It is hardly necessary, however, to cite the numerous instances of modification or arrest of the secretion from this cause, which are quoted in many works. Vernois and Bec-

[1] *Cyclopædia of Anatomy and Physiology*, London, 1839–1847, vol. iii., p. 362.

querel mention a very striking case, in which a hospital wet-nurse, who had lost her only child from pneumonia, became violently affected with grief, and presented, as a consequence, an immediate diminution in the quantity of her milk, with a great reduction in the proportion of salts, sugar, and butter. In this case the proportion of caseine was increased.[1] Sir Astley Cooper mentions two cases in which the secretion of milk was instantaneously and permanently arrested from terror.[2] These cases are types of numerous others, which have been reported by writers, of the effects of mental emotions upon secretion.

In the present state of our knowledge, we can only comprehend the influence of mental emotions upon secretion, by assuming that they operate through the nervous system; and in many of the glands, the influence of the nerves has been clearly demonstrated by actual experiment. Direct observations, however, upon the influence of the nerves upon the mammary glands are few and unsatisfactory. The operation of dividing the nerves distributed to these glands, which has occasionally been practised upon animals in lactation, has not been observed to produce any sensible diminution in the quantity of the secretion.[3] It is difficult, however, to operate upon all the nerves distributed to these organs.

Quantity of Milk.—It is very difficult to form a reliable estimate of the average quantity of milk secreted by the human female in the twenty-four hours. The amount undoubtedly varies very much in different persons; some women being able to nourish two children, while others, though apparently in perfect health, furnish hardly enough food for one.

[1] VERNOIS ET BECQUEREL, *Du lait chez la femme dans l'état de santé et dans l'état de maladie*, Paris, 1853, p. 73.

[2] COOPER, *The Anatomy and Diseases of the Breast*, Philadelphia, 1845, p. 101.

[3] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 291.

Cooper, as the result of direct observation, states that the quantity that can be drawn from a full breast is usually about two fluidounces.[1] This may be assumed to be about the quantity contained in the lactiferous ducts when they are moderately distended. Lehmann, taking for the basis of his calculations the observations of Lampérierre,[2] who found, as the result of sixty-seven experiments, that from fifty to sixty grammes of milk were secreted in two hours, estimates that the average quantity discharged in twenty-four hours is 1,320 grammes, or about 44·5 fluidounces.[3] Robin estimates that the daily quantity is from thirty-four to one hundred fluidounces;[4] but he does not give the data from which this estimate is formed. Taking into consideration the evident variations in the quantity of milk secreted by different women, it may be assumed that the daily production is from two to six pints.

Certain conditions of the female are capable of materially influencing the quantity of milk secreted. It is evident that the secretion is usually somewhat increased within the first few months of lactation, when the progressive development of the child demands an increase in the quantity of nourishment. If the menstrual function become re-established during lactation, the milk is usually diminished in quantity during the periods, but sometimes it is not affected, either in its quantity or composition. Should the female become pregnant, there is generally a great diminution in the quantity of milk, and that which is secreted is ordinarily regarded as possessing little nutritive power. In obedience to a popular prejudice, apparently well-founded, the child is usually taken from the breast as soon as pregnancy is recognized. All of these conditions have been

[1] Cooper, *The Anatomy and Diseases of the Breast*, Philadelphia, 1845, p. 93.

[2] Lampérierre, *Des moyens à reconnaitre la quantité et la qualité de la sécrétion lactée chez la femme.—Comptes rendus*, Paris, 1850, tome xxx., p. 174.

[3] Lehmann, *Physiological Chemistry*, Philadelphia, 1855, vol. ii., p. 63.

[4] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 402.

closely studied by Vernois and Becquerel, with reference to their influence upon the composition of the milk; and their observations will be fully considered in treating of the chemistry of the mammary secretion. Authors have not noted any marked and constant variations in the quantity of milk in females of different ages.

Properties and Composition of the Milk.

The general appearance and characters of ordinary cow's milk are sufficiently familiar and may serve as a standard for comparison with the milk of the human female.[1] Human milk is not so white nor so opaque as cow's milk, having ordinarily a slightly bluish tinge. The milk of different healthy women presents some variation in this regard. After the secretion has become fully established, the fluid possesses no viscidity, and is nearly opaque. It is almost inodorous, of a peculiar soft and sweetish taste, and when perfectly fresh, has a decidedly alkaline reaction. The taste of human milk is sweeter than that of cow's milk. A short time after its discharge from the gland, the reaction of milk becomes faintly acid; but this change takes place more slowly in human milk than in the milk of most of the inferior animals.

The average specific gravity of human milk, according to Vernois and Becquerel, is 1032; though this is subject to considerable variation, the minimum of eighty-nine observations being 1025, and the maximum, 1046.[2] The observations of most physiological chemists have shown that this average is nearly correct.

Milk is not coagulated by heat, even after prolonged boiling; but a thin pellicle then forms on the surface, which is probably due to the combined action of heat and the at-

[1] The properties and composition of cow's milk have already been considered in another volume. See vol. ii., Alimentation, p. 77, *et seq.*

[2] VERNOIS ET BECQUEREL, *Du lait chez la femme*, Paris, 1853, p. 14.

mosphere upon the caseine. Although a small quantity of albumen exists in the milk, this does not coagulate on the surface by the action of heat, for the scum does not form when the fluid is heated in an atmosphere of carbonic acid, or of hydrogen, or in a vacuum.[1]

When the milk is coagulated by any substance acting upon the caseine, or when it coagulates spontaneously, it separates into a curd, composed of caseine with most of the fatty particles, and a nearly-clear, greenish-yellow serum, called whey. This separation occurs spontaneously, at a variable time after the discharge of the milk, taking place much more rapidly in warm than in cold weather. It is a curious fact that fresh milk is frequently coagulated during a thunder-storm, a phenomenon which has never been satisfactorily explained.

On being allowed to stand for a short time, the milk separates, without coagulating, into two tolerably-distinct portions. A large proportion of the globules rise to the top, forming a yellowish-white, and very opaque fluid, called cream, leaving the lower portion poorer in globules and of a decidedly bluish tint. In healthy milk the stratum of cream forms from one-fifth to one-third of the entire mass of the milk. In the human subject the skim-milk is not white and opaque, but is nearly as transparent as the whey. This is a very good method of testing the richness of milk; and little graduated glasses, called lactometers, have been constructed for measuring the thickness of the layer of cream. The specific gravity of the cream from milk of the average specific gravity of 1032 is about 1024. The specific gravity of the skim-milk is about 1034.

Microscopical Characters of the Milk.—If a drop of milk be examined with a magnifying power of from three hundred to six hundred diameters, the cause of its opacity will be apparent. It contains an immense number of minute

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 388.

globules, of great refractive power, held in suspension in a clear fluid. These are known under the name of milk-globules, and are composed of margarine, oleine, and a fatty matter, peculiar to milk, called butyrine. In human milk the particles are perfectly spherical; but in cow's milk they are often polyhedric from mutual compression. This difference is due to the softer consistence of the butter in human milk, the globules containing a much larger proportion of oleine; and if cow's milk be warmed, the particles also assume a spherical form.

The human milk-globules measure from $\frac{1}{25000}$ to $\frac{1}{1250}$ of an inch in diameter. They are usually distinct from each other, but may occasionally become collected into groups without indicating any thing abnormal. In a perfectly normal condition of the glands, when the lacteal secretion has become fully established, the milk contains nothing but a clear fluid with these globules in suspension. The proportion of fatty matter in the milk is from twenty-five to forty-eight parts per thousand, and this gives an idea of the proportion of globules which are seen on microscopical examination.

There has been a great deal of discussion with regard to the anatomical constitution of the milk-globules. In many late works it is stated that they are true anatomical elements, composed of fatty matters surrounded by an albuminoid membrane; but other writers assume that the fat is merely in the form of an emulsion, and is simply divided into globules and held in suspension, like the fatty particles of the chyle. No one, however, has assumed to have seen the investing membrane of the milk-globules, and its existence is only inferred from the behavior of these little particles in the presence of certain reagents.

It is unnecessary to review in detail the numerous opinions that have been advanced on this subject. As far as can be ascertained by simple examination, even with the highest magnifying powers, the globules appear perfectly

homogeneous; and the burden of proof rests with those who profess to be able to demonstrate the existence of an investing membrane. Robin, one of the highest authorities on these subjects, argues against the existence of a membrane, and opposes the observations of those who assume to have demonstrated it by explanations of the phenomena produced by reagents, which do not involve, as a necessity, the presence of such a structure. The arguments in favor of its existence are not very satisfactory; and the experiments upon which they are based relate chiefly to the action of ether upon the globules before and after the action of other reagents.

If a quantity of milk be shaken up with an equal volume of ether, the mixture remains opaque; but if a little potash be added, the fatty matters are dissolved, and the mixture then becomes more or less clear. These facts are all that can be observed without following out the changes with the microscope. Robin has shown that the fatty particles are acted upon when the milk is thoroughly agitated with ether alone; and that the opacity is then due to the fact that the ether, with the fat in solution, is itself in the form of an emulsion. If the opaque mixture of milk and ether be examined with the microscope, globules are seen, larger than the ordinary milk-globules, much paler, and possessing much less refractive power. These he supposes to be composed of fat and ether. If potash be added, either before or after the addition of ether, the constitution of the whole mass of liquid is changed, and it becomes somewhat transparent, though by no means perfectly clear.[1] It is assumed that, in the first instance, the ether does not attack the globules, because it has no effect upon the membrane which is supposed to exist, and that the potash acts upon the membrane, allowing the ether then to take up the fat; but if the observations of Robin be correct, it is evident that this view cannot be sustained.

If dilute acetic acid be added to a specimen of milk under

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 390, *et seq.*

the microscope, the globules become deformed, and some of them show a tendency to run together; an appearance which is supposed by Henle, who was the first to study closely the action of acetic acid upon the milk-globules, to indicate the existence of a membrane.[1] This deduction, however, is not justifiable. Acetic acid readily coagulates the caseine, a principle which is most efficient in maintaining the fat in its peculiar condition. The coagulating caseine then presses upon the globules, and produces, in this way, all the changes in form that have been observed.

Most of the other arguments in favor of the existence of a membrane have no support in direct observation, and consequently do not demand special consideration; while all the facts which we have been able to find relating to this subject go to show that the fatty matters in the milk are in the condition of a simple emulsion. The precise condition, however, of the fluid immediately surrounding the globules is not fully understood. Certain of the constituents of fluids capable of forming emulsive mixtures with liquid fats may form a coating of excessive tenuity immediately around the globules, but they never constitute distinct membranes capable of resisting the action of solvents upon the fats; and, in the case of the milk, they do not prevent the mechanical union of the globules into masses, as occurs in the process of churning.

Milk-globules less than $\frac{1}{5000}$ of an inch in diameter present under the microscope that peculiar oscillating motion known as the Brownian movement. This is arrested on the addition of acetic acid, by coagulation of the caseine.

From these facts, it is evident that the milk-globules are composed simply of fat in the condition of a fine emulsion. They are not true anatomical elements, originating by a process of genesis in a blastema, undergoing physiological decay, and capable of self-regeneration from materials furnished by the menstruum in which they are suspended, like

[1] HENLE, *Traité d'anatomie générale*, Paris, 1843, tome ii., p. 521.

the blood-corpuscles or leucocytes. They are simply elements of secretion.

Composition of the Milk.—We do not propose, in treating of the composition of the milk, to consider the various methods of analysis which have been employed by different chemists. The only constituent that has ever presented much difficulty in the estimation of its quantity is caseine; but the various processes now employed in its extraction lead to nearly the same results. The following table, compiled by Robin from the analyses of various chemists, gives the constituents of human milk.[1]

Composition of Human Milk.

Water		902·717	to	863·149
Caseine (desiccated)		29·000	"	39·000
Lacto-proteine		1·000	"	2·770
Albumen		traces	"	0·880
Butter, 25 to 38	Margarine	17·000	"	25·840
	Oleine	7·500	"	11·400
	Butyrine, Caprine, Caproïne, Capriline	0·500	"	0·760
Sugar of milk (Lactine, or lactose)		37·000	"	49·000
Lactate of soda (?)		0·420	"	0·450
Chloride of sodium		0·240	"	0·340
Chloride of potassium		1·440	"	1·830
Carbonate of soda		0·053	"	0·056
Carbonate of lime		0·069	"	0·070
Phosphate of lime of the bones		2·310	"	3·440
Phosphate of magnesia		0·420	"	0·640
Phosphate of soda		0·225	"	0·230
Phosphate of iron (?)		0·032	"	0·070
Sulphate of soda		0·074	"	0·075
Sulphate of potassa			traces.	
		1,000·000		1,000·000

Gases in solution	Oxygen	1·29	30 parts per 1,000 in volume.[2]
	Nitrogen	12·17	
	Carbonic acid	16·54	

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 395. In copying this table, the arrangement has been somewhat modified, and an evident arithmetical error has been corrected.

[2] HOPPE, *Untersuchungen über die Bestandtheile der Milch und ihre nächsten*

The proportion of water in milk is subject to a certain amount of variation, but this is not so considerable as might be expected from the great variations in the entire quantity of the secretion. In treating of the quantity of milk in the twenty-four hours, we have seen that the influence of drinks, even when nothing but pure water has been taken, is very marked; and although the activity of the secretion is much increased by fluid ingesta, the quality of the milk is not usually affected, and the proportion of water to the solid matters remains about the same.

Nitrogenized Constituents of Milk.—Very little remains to be said concerning the nitrogenized constituents of human milk after what has been stated with regard to the composition of cow's milk, in another volume.[1] The different principles of this class undoubtedly have the same nutritive function, and appear to be identical in all varieties of milk, the only difference being in their relative proportion. It is a matter of common experience, indeed, that the milk of many of the lower animals will take the place of human milk, when prepared so as to make the proportions of its different constituents approximate the composition of the natural food of the child. A comparison of the composition of human milk and cow's milk shows that the former is poorer in nitrogenized matters, and richer in butter and sugar; and consequently, the upper strata of cow's milk, appropriately sweetened and diluted with water, very nearly represent the ordinary breast-milk.

Caseine is by far the most important of the nitrogenized principles of milk, and supplies nearly all of this kind of

Zersetzungen.—VIRCHOW's *Archiv*, Berlin, 1859, Bd. xvii., S. 439. The observations of Hoppe were made upon goat's milk, and in the apparatus used, the milk was drawn directly into the receiver and carefully protected from contact with the air. Hoppe criticises the observations of Lehmann and Vogel as probably incorrect, the fluid not being sufficiently protected from the atmosphere, which gives, according to Hoppe, an excess in the proportion of oxygen.

[1] See vol. ii., Alimentation, p. 77, *et seq.*

nutritive matter demanded by the child. Lacto-proteine,[1] a principle described by Millon and Commaille, is not so well defined, and albumen exists in the milk in very small quantity. That albumen always exists in milk can readily be shown by the following process described by Bernard: If milk, treated with an excess of sulphate of magnesia so as to form a thin paste, be thrown upon a filter, the caseine and fatty matters will be retained, and the clear liquid that passes through shows a marked opacity upon the application of heat or the addition of nitric acid.[2]

The coagulation of milk depends upon the reduction of the caseine from a liquid to a semisolid condition. When milk is allowed to coagulate spontaneously, or sour, the change is effected by the action of the lactic acid which results from a transformation of a portion of the sugar of milk. Caseine, in fact, is coagulated by any of the acids, even the feeble acids of organic origin. It differs from albumen in this regard, and in the fact that it is not coagulated by heat. It has been suggested that in fresh milk the caseine exists in combination with carbonate of soda, and that coagulation always takes place from the action of acids upon this salt, by which the caseine is set free. It is true that coagulated caseine may be readily dissolved in a solution of carbonate of soda, but it has been shown by the experiments of Selmi, that coagulation may be induced by the agency of certain neutral principles, while the milk retains its alkaline reaction. If fresh milk be slightly raised in temperature, and be treated with an infusion of the gastric mucous membrane of the calf, coagulation will take place in from five to ten minutes, the clear liquid still retaining its alkaline reaction.[3] This observation has been repeatedly confirmed. Simon

[1] Millon et Commaille, *Nouvelle substance albumioïde contenue dans le lait.—Comptes rendus*, Paris, 1864, tome lix., p. 301.

[2] Bernard, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 224.

[3] Selmi, *Recherches sur l'action de la présure dans la coagulation du lait.—Journal de pharmacie et de chimie*, Paris, 1846, 3me série, tome ix., p. 265.

has also found that the mucous membrane of the stomach of an infant a few days old, that had recently died, coagulated woman's milk more readily than the mucous membrane of the stomach of the calf.[1]

Non-Nitrogenized Constituents of Milk.—Non-nitrogenized matters exist in abundance in the milk. The liquid caseine and the water hold the fats, as we have seen, in the condition of a fine and permanent emulsion. This fat has been separated from the milk and analyzed by chemists, and is known under the name of butter. In human milk, the butter is much softer than in the milk of many of the inferior animals, particularly the cow; but it is composed of essentially the same constituents, though in different proportions. In different animals there are developed, even after the discharge of the milk, certain odorous principles, more or less characteristic of the animal from which the butter is taken.

The greatest part of the butter consists of margarine. It contains, in addition, oleine, with a small quantity of peculiar fats, not very well determined, called butyrine, caprine, caproïne, and capriline. The margarine and oleine are principles found in the fat throughout the body; but the last-named substances are peculiar to the milk. These are especially liable to acidification, and the acids resulting from their decomposition give the peculiar odor and flavor to rancid butter.[2] Bromeis estimated the different constituents of the butter from cow's milk, and found it to contain sixty-eight parts of margarine, thirty parts of oleine, and two parts of butyrine, capronine, and caprine.[3]

[1] SIMON, *Animal Chemistry with Reference to the Physiology and Pathology of Man*, Philadelphia, 1846, p. 333.

[2] Butyrine was discovered, and the changes which it is liable to undergo were first described by Chevreul. (*Faits pour servir à l'histoire du beurre de vache. Extraits d'un mémoire lu à l'Académie des Sciences*, le 14 juin, 1819. —*Annales de chimie et de physique*, Paris, 1823, tome xxii., p. 373.)

[3] BROMEIS, *Ueber die in der Butter enthaltenen Fette und fetten Saüren.—An-*

Sugar of milk, sometimes called lactine, or lactose, is the most abundant of the solid constituents of the mammary secretion. It is this principle that gives to the milk its peculiar sweetish taste, though this variety of sugar is much less sweet than cane-sugar. The chief peculiarities of milk-sugar are, that it readily undergoes change into lactic acid in the presence of nitrogenized ferments, and takes on alcoholic fermentation slowly and with difficulty. At one time, indeed, it was supposed that milk-sugar could not be decomposed into alcohol and carbonic acid; but it is now well established that this change can be induced, the only peculiarity being that it takes place very slowly. In some parts of the world, intoxicating drinks are made by the alcoholic fermentation of milk. Milk-sugar is composed of $C_{12}H_{12}O_{12}$ and responds to the ordinary tests for the animal varieties of sugar.

A consideration of the nutritive action of the fatty and saccharine constituents of milk belongs properly to the subjects of alimentation and nutrition. It may be stated here, however, that these principles seem to be as necessary to the nutrition of the child as the nitrogenized principles; though the precise manner in which they affect the development and regeneration of the tissues has not been ascertained.

Inorganic Constituents of Milk.—It is probable that many inorganic principles exist in the milk which are not given in the table; and the separation of these principles from their combinations with organic matters is one of the most difficult problems in physiological chemistry. This must be the case, for during the first months of extra-uterine

nalen der Chemie und Pharmacie, Heidelberg, 1842, B. xlii., S. 70. The above is an approximative estimate of the proportions of the various fatty constituents of butter, deduced from the quantities of fatty acids obtained. Bromeis, like many chemists of that day, supposed that the neutral fats were composed of the fatty acids combined with glycerine, or the oxide of glycile. It is now generally admitted that the fatty acids and glycerine are formed by actual decomposition, and do not exist in combination in the neutral fats.

existence, the child derives all the inorganic, as well as the organic matters necessary to nutrition and development, from the breast of the mother. The reaction of the milk depends upon the presence of the alkaline carbonates, and these principles are important in preserving the fluidity of the caseine. It is not determined precisely in what form iron exists in the milk, but its presence here is undoubted A comparison of the composition of the milk with that of the blood will show that most of the important inorganic principles found in the latter fluid exist also in the milk.

Hoppe has indicated the presence of carbonic acid, nitrogen, and oxygen, in solution, in milk.[1] Of these gases, carbonic acid is the most abundant. It is well known that the presence of gases in solution in liquids renders them more agreeable to the taste, and carbonic acid increases very materially their solvent properties. Aside from these considerations, the precise function of the gaseous constituents of the milk is not apparent.

A study of the composition of the milk fully confirms the fact, which we have already had occasion to state, that this is a typical alimentary fluid, and presents in itself the proper proportion and variety of material for the nourishment of the body during the period when the development of the system is going on with its maximum of activity. The form in which its different nutritive constituents exist is such that they are easily digested and are assimilated with great rapidity.

Variations in the Composition of the Milk.

The most elaborate researches concerning the variations in the composition of the milk are those of Vernois and Becquerel. Their observations relate to the composition of milk both in health and disease; but we shall consider

[1] *Loc. cit.*

only the differences this fluid has been found to present under varying normal conditions. Vernois and Becquerel have indicated a certain amount of variation at different ages and at different periods in lactation, but they show, at the same time, that the fluid is not subject to changes in its composition sufficiently great to influence materially the nutrition of the child.

If the composition of the milk be compared at different periods of lactation, it will be found to undergo great changes during the first few days. In fact, the first fluid secreted after parturition is so different from other milk, that it has been called by another name. It is then known as colostrum, the peculiar properties of which will be considered more fully hereafter under a distinct head. As the secretion of milk becomes established, the fluid, from the first to the fifteenth day, becomes gradually diminished in density and in its proportion of water and of sugar, while there is a progressive increase in the proportion of most of the other constituents; viz., butter, caseine, and the inorganic salts.[1] The milk, therefore, as far as we can judge from its composition, as it increases in quantity during the first few days of lactation, is constantly increasing in its nutritive properties.

The differences in the composition of the milk, taken from month to month during the entire period of lactation, are not so distinctly marked. It is difficult, indeed, to indicate any constant variations of sufficient importance to lead to the view that the milk varies much in its nutritive properties at different times, within the ordinary period of lactation.

If we except the first few months, the secretion is not found to present any constant variations in density. Vernois and Becquerel found a notable increase in the proportion of solid matters from the first to the third month; the sugar was increased from the eighth to the tenth month; the ca-

[1] Vernois et Becquerel, *Du lait chez la femme*, Paris, 1853, p. 24.

seine was increased from the first day to the second month, inclusive, and diminished from the tenth to the twenty-fourth month; there was a constant and considerable increase in the proportion of butter, from the first day to the fifth month, and a diminution from the fifth to the sixth, and from the tenth to the eleventh month; there was a slight, feeble, but almost constant and progressive increase in the proportion of salts from the first day to the fifth month, and a diminution at all other periods.[1]

The differences noted between the milk of primiparæ and multiparæ were very slight and not very important. As a rule, however, the milk of primiparæ approached more nearly the normal standard.

The menstrual periods, when they occur during lactation, have been found by most observers to modify considerably the composition and properties of the milk; and it is well known to practical physicians that the secretion is then liable to produce serious disturbances of the digestive system of the child, though frequently these effects are not observed. The changes in the composition of the milk which commonly occur during menstruation are, great increase in the quantity of caseine, increase in the proportion of butter and the inorganic salts, and a slight diminution in the proportion of sugar. The common impression that the milk is unfit for the nourishment of the child if pregnancy occur during lactation is undoubtedly well-founded, though analyses of the milk of pregnant women have never been made on an extended scale. Vernois and Becquerel made but one examination of this kind, at the third month of gestation, and found a great increase in the proportion of butter, slight increase in sugar and the inorganic salts, and a slight diminution in the proportion of caseine.[2]

The question is frequently discussed by physiological writers, whether the milk of fair women is different from that of brunettes. There are hardly sufficient data, however,

[1] *Op. cit.*, p. 31. [2] *Op. cit.*, p. 38.

to form a definite opinion upon this subject. The analyses of L'Héritier,[1] and Vernois and Becquerel,[2] indicate a greater proportion of most of the solid matters in the milk of brunettes, with a very slight difference in the proportion of butter in favor of blondes. Almost all authorities who have expressed an opinion upon this question give the preference to the milk of brunettes. Donné, however, expresses himself very decidedly against the popular prejudice in favor of brunettes as nurses. "As regards the color of the skin and the hair, the results at which I have arrived in nowise justify the generally-received popular prejudice in favor of brunettes; in more than four hundred nurses, I found no sensible difference in favor of brunettes over blonde women or over those with chestnut hair; but of nine red-haired women, five only presented the proper qualities."[3] It would be interesting in this connection to determine whether there be any marked difference in the milk of the black and the white race, particularly as it has long been the custom in some parts of the United States to permit white children to be nursed by black women. Infants that are nourished in this way apparently thrive as well as those nursed by white women; and there is no reason to suppose that there is any difference in the milk of the two races. Sir Astley Cooper mentions some interesting facts concerning the black women of the West Indies, communicated to him by his nephew, Dr. Young, which show that

[1] L'Héritier, *Traité de chimie pathologique*, Paris, 1842, p. 638; Vernois et Becquerel, *op. cit.*, p. 52.

[2] L'Héritier was the first to compare critically the milk of blondes with that of brunettes. In two women, twenty-two years of age, and subjected to the same regimen, the milk of the brunette contained much more caseine, butter, sugar, and salts, than the milk of the blonde; but these two instances presented the extremes of difference; and as the mean of all his observations, it was found that the difference was comparatively slight. Vernois and Becquerel arrived at essentially the same results, except that the proportion of butter was a little greater in the milk of fair women.

[3] Donné, *Cours de microscopie*, Paris, 1844, p. 409.

there is probably no difference between the milk of the blacks and of Europeans.[1]

In normal lactation, there is no marked and constant difference in the composition of milk that has been secreted in great abundance, and milk which is produced in comparatively small quantity; nor do we observe that difference between the milk first drawn from the breast and that taken when the ducts are nearly empty, which is observed in the milk of the cow.[2]

The influence of alimentation and the taking of liquids upon lactation relate chiefly to the quantity of milk, and have already been considered.[3]

In treating of the influences which modify the secretion of milk, we have already alluded to the effects of violent mental emotions upon the production and the composition of this fluid. The very remarkable case of profound alteration of the milk by violent grief, detailed by Vernois and Becquerel, is the only one in which the secretion in this condition has been carefully analyzed. The changes thus produced in its composition have already been referred to,[4] the most marked difference being observed in the proportion of butter, which became reduced from 23·79 to 5·14 parts per 1,000.

Colostrum.

Near the end of utero-gestation, during a period which varies considerably in different women and has not been accurately determined, a small quantity of a thickish, stringy fluid may frequently be drawn from the mammary glands. This bears little resemblance to perfectly-formed milk. It is small in quantity, and is usually more abundant in multiparæ than in primiparæ. This fluid, with that secreted for

[1] COOPER, *The Anatomy and Diseases of the Breast*, Philadelphia, 1845, p. 103, *et seq.*

[2] See vol. ii., Alimentation, p. 79.

[3] See page 83. [4] See page 86.

the first few days after delivery, is called colostrum. It is yellowish, semiopaque, of a distinctly alkaline reaction, and somewhat mucilaginous in its consistence. Its specific gravity is considerably above that of the ordinary milk, being from 1040 to 1060. As lactation progresses, the character of the secretion rapidly changes, until it becomes loaded with true milk-globules and assumes the characters of ordinary milk.

The opacity of the colostrum is due to the presence of a number of different corpuscular elements. Milk-globules, very variable in size and number, are to be found in the secretion from the first. These, however, do not exist in sufficient quantity to render the fluid very opaque, and they are frequently aggregated in rounded and irregular masses, held together, apparently, by some glutinous matter. Peculiar corpuscles, first accurately described by Donné, under the name of "granular bodies," and supposed to be characteristic of the colostrum, always exist in this fluid.[1] These are now known as colostrum-corpuscles. They are spherical, varying in size from $\frac{1}{2500}$ to $\frac{1}{800}$ of an inch, are sometimes pale, but more frequently quite granular, and contain very often a large number of fatty particles. They behave in all respects like leucocytes, and are described by Robin as a variety of these bodies.[2] Many of them are precisely like the leucocytes found in the blood, lymph, or pus. Their appearance was very well described by Donné, who supposed that they were mucus-corpuscles.[3] We now know, however, that the so-called mucus-corpuscle does not differ from the pus-corpuscle or the white corpuscle of the blood; and leucocytes generally, when confined in liquids that are not subject to movements, are apt to undergo enlargement, to become fatty, and, in short, present all the different appearances observed in the colostrum-corpuscles. In addition

[1] DONNÉ, *Cours de microscopie*, Paris, 1844, p. 400.

[2] ROBIN, *Sur quelques points de l'anatomie et de la physiologie des leucocytes.—Journal de la physiologie*, Paris, 1859, tome ii., p. 50.

[3] DONNÉ, *loc. cit.*

to these corpuscular elements, a small quantity of mucosine may frequently be observed in the colostrum, on microscopical examination.

On the addition of ether to a specimen of colostrum under the microscope, most of the fatty particles, both within and without the colostrum-corpuscles, are dissolved. Ammonia added to the fluid renders it stringy, and sometimes the entire mass assumes a gelatinous consistence.

In its proximate composition, the colostrum presents many points of difference from true milk. It is sweeter to the taste, and contains a greater proportion of sugar and of the inorganic salts. The proportion of fat is at least equal to the proportion in the milk, and is generally greater. Instead of caseine, the pure colostrum contains a large proportion of albumen; and as the character of the secretion changes in the process of lactation, the albumen becomes gradually reduced in quantity and caseine takes its place.

Without referring in detail to the numerous analyses of colostrum in the human subject and in the inferior animals, by Simon, Lassaigne, and others, the following, deduced from the analyses of Clemm, may be taken as the ordinary composition of this fluid in the human female:

Composition of the Colostrum.[1]

Water	945·24
Albumen, and salts insoluble in alcohol	29·81
Butter	7·07
Sugar of milk, extractive matter, and salts soluble in alcohol	17·27
Loss	0·61
	1,000·00

Colostrum ordinarily decomposes much more readily than milk, and takes on putrefactive changes very rapidly. If it be allowed to stand for from twelve to twenty-four hours, it sep-

[1] CLEMM, *Inquisitiones in Mulierum ac Bestiarum complurium Lac*, Gottingae, 1845, p. 14.

erates into a thick, opaque, yellowish cream and a serous fluid. In an observation by Sir Astley Cooper, nine measures of colostrum, taken soon after parturition, after twenty-four hours of repose, gave six parts of cream to three of milk.[1]

The peculiar constitution of the colostrum, particularly the presence of an excess of sugar and inorganic salts, renders it somewhat laxative in its effects, and it is supposed to be useful, during the first few days after delivery, in assisting to relieve the infant of the accumulation of meconium.

As the quantity of colostrum that may be pressed from the mammary glands during the latter periods of utero-gestation, particularly the last month, is very variable, it becomes an interesting and important question to determine whether this secretion have any relation to the quantity of milk that may be expected after delivery. This has been made the subject of careful study by Donné, who arrived at the following important conclusions:

In women in whom the secretion of colostrum is almost absent, the fluid being in exceedingly small quantity, viscid, and containing hardly any corpuscular elements, there is hardly any milk produced after delivery.

In women who, before delivery, present a moderate quantity of colostrum, containing very few milk-globules and a number of colostrum-corpuscles, after delivery the milk will be scanty or it may be abundant, but it is always of poor quality.

But when the quantity of colostrum produced is considerable, the secretion being quite fluid and rich in corpuscular elements, particularly milk-globules, the milk after delivery is always abundant and of good quality.[2]

From these observations it would seem that the production of colostrum is an indication of the proper development of the mammary glands; and the early production of fatty

[1] Cooper, *The Anatomy and Diseases of the Breast*, Philadelphia, 1845, p. 85.
[2] Donné, *op. cit.*, p. 407, *et seq.*

granules, which are first formed by the cells lining the secreting vesicles, indicates the probable activity in the secretion of milk after lactation has become fully established.

The secretion of the mammary glands preserves the characters of colostrum until toward the end of the milk-fever, when the colostrum-corpuscles rapidly disappear, and the milk-globules become more numerous, regular, and uniform in size. It may be stated in general terms that the secretion of milk becomes fully established and all the characters of the colostrum disappear from the eighth to the tenth day after delivery. A few colostrum-corpuscles and masses of agglutinated milk-globules may sometimes be discovered after the tenth day, but they are very rare; and after the fifteenth day the milk does not sensibly change in its microscopical or its chemical characters.

Lacteal Secretion in the Newly-Born.

It is a curious fact that in infants of both sexes there is generally a certain amount of secretion from the mammary glands, commencing at birth, or from two to three days after, and continuing sometimes for two or three weeks. The quantity of fluid that may be pressed out at the nipples at this time is very variable. Sometimes only a few drops can be obtained, but occasionally the fluid amounts to one or two drachms. Although it is impossible to indicate the object of this secretion, which takes place when the glands are in a rudimentary condition, it has been so often observed and described by physiologists that there can be no doubt with regard to the nature of the fluid, and the fact that the secretion is almost always produced in greater or less quantity.

The latest researches upon this subject are those of Gubler and Quevenne, who have given a tolerably complete analysis of the fluid. The fact of the almost constant occurrence of the secretion was fully established, in 1853, by

Guillot.[1] The following is an analysis by Quevenne of the secretion obtained by Gubler. The observations of Gubler were very extended, and were made upon about twelve hundred children. The secretion rarely continued more than four weeks, but in four instances it persisted for two months.[2]

Composition of the Milk of the Infant.

Water	894·00
Caseine	26·40
Sugar of milk	62·20
Butter	14·00
Earthy phosphates	1·20
Soluble salts (with a small quantity of insoluble phosphates).	2·20
	1,000·00

This fluid does not differ much in its composition from ordinary milk. The proportion of butter is much less, but the amount of sugar is greater, and the quantity of caseine is nearly the same.

Of the other fluids which are enumerated in the list of secretions, the saliva, gastric juice, pancreatic juice, and the intestinal fluids have already been considered in connection with digestion.[3] The physiology of the lachrymal secretion will be taken up in connection with the eye, and the bile will be treated of fully under the head of excretion.

[1] GUILLOT, *De la sécrétion du lait chez les enfants nouveau-nés, et des accidents qui peuvent l'accompagner.—Archives générales*, Paris, 1853, 5me série, tome ii., p. 513, *et seq.*

[2] GUBLER, *Mémoire sur la sécrétion et la composition du lait chez les enfants nouveau-nés des deux sexes.—Comptes rendus et mémoires de la Société de Biologie*, 2me, 1855, Paris, 1856, p. 289.

[3] See vol. ii., Digestion.

CHAPTER IV.

EXCRETION—ACTION OF THE SKIN.

Differences between the secretions proper and the excretions—Composition of the excretions—Mode of production of the excretions—Discharge of the excretions—Physiological anatomy of the skin—Extent and thickness of the skin—Layers of the skin—The corium, or true skin—The epidermis and its appendages—Desquamation of the epidermis—Physiological anatomy and uses of the nails and hair—Development and growth of the nails—Varieties of hair—Number of the hairs—Roots of the hairs, and hair-follicles—Structure of the hairs—Sudden blanching of the hair—Uses of the hairs—Perspiration—Sudoriparous glands—Mechanism of the secretion of sweat—Quantity of cutaneous exhalation—Properties and composition of the sweat—Peculiarities of the sweat in certain parts.

In entering upon the study of the elimination of effete matters, it is necessary to appreciate fully the broad distinctions between the secretions proper and the excretions, in their composition, the mechanism of their production, and their destination. These considerations are again referred to,[1] for the reason that they have not ordinarily received that attention in works upon physiology which their importance demands. The mechanism of excretion is inseparably connected with the function of nutrition, and forms one of the great starting-points in the study of all the modifications of nutrition in diseased conditions.

Taking the urine as the type of the excrementitious fluids, it is found to contain none of those principles included in the class of non-crystallizable, organic nitrogenized matters, but is composed entirely of crystallizable matters simply

[1] See chapter I. on "Secretion in General."

held in solution in water. The character of these principles depends upon the constitution of the blood and the general condition of nutrition, and not upon any formative action in the glands. The principles themselves represent the ultimate physiological changes of certain constituent parts of the living organism, and are in such a condition that they are of no farther use in the economy and are simply discharged from the body. Certain inorganic matters are found in the excrementitious fluids, are discharged with the products of excretion, and are thus associated with the organic principles of the economy in their physiological destruction, as well as in their deposition in the tissues. Coagulable organic matters, such as albumen or fibrin, never exist in the excrementitious fluids under normal conditions; except as the products of other glands may become accidentally or constantly mixed with the excrementitious fluids proper. The same remark applies to the non-nitrogenized matters (sugars and fats), which, whether formed in the organism or taken as food, are consumed as such in the process of nutrition. The production of the excretions is constant, being subject only to certain modifications in activity, dependent upon varying conditions of the system. All of the elements of excretion preëxist in the blood, either in the precise condition in which they are discharged, or in some slightly modified form.

Under the head of excretion, it is proposed to consider the general properties and composition of the different excrementitious fluids; but the relations of the excrementitious matters themselves to the tissues will be more fully treated of in connection with nutrition.

The urine is a purely excrementitious fluid. The perspiration and the secretion of the axillary glands are excrementitious fluids, but contain a certain amount of the secretion of the sebaceous glands. Certain excrementitious matters are found in the bile, but at the same time, this fluid contains principles manufactured in the liver, and has

an important function as a secretion, in connection with the process of digestion.

Physiological Anatomy of the Skin.

The skin is one of the most complex and important structures in the body, and possesses a variety of functions. In the first place it forms a protective covering for the general surface. It is quite thick over the parts most subject to pressure and friction, is elastic over movable parts and those liable to variations in size, and in many situations is covered with hair, which affords an additional protection to the subjacent structures. The skin and its appendages are bad conductors of caloric, are capable of resisting very considerable variations in temperature, and thus tend to maintain the normal standard of the animal heat. As an organ of tactile sensibility, the skin has an important function, being abundantly supplied with sensitive nerves, some of which present an arrangement peculiarly adapted to the nice appreciation of external impressions. The skin assists in preserving the external forms of the muscles; it relieves the abrupt projections and depressions of the general surface, and gives roundness and grace to the contours of the body. In some parts it is very closely attached to the subjacent structures, while in others it is less adherent, and is provided with a layer of adipose tissue.

As an organ of excretion, the skin is very important; and although the quantity of excrementitious matter exhaled from it is not very great, and probably not subject to much variation, the evaporation of water from the general surface is always considerable, and is subject to such modifications as may become necessary from the varied conditions of the animal temperature. Thus, while the skin protects the body from external influences, its function is important in regulating the heat produced as one of the numerous phenomena attendant upon the general process of nutrition.

As the skin presents such a variety of functions, its physiological anatomy is most conveniently considered in connection with different divisions of the subject of physiology. For example, under the head of secretion, we have already taken up the structure of the different varieties of sebaceous glands. The anatomy of the skin as an organ of touch will be most appropriately considered in connection with the nervous system. In this connection we shall describe the excreting organs found in the skin; and here it will be most convenient to study briefly its general structure and the most important points in the anatomy of the epidermic appendages. A full and connected description of the skin and its appendages belongs properly to works upon anatomy.

General Appearance of the Skin.—It is unnecessary to discuss very minutely the general appearance of the skin. Its color is sufficiently familiar. The tissue of the true skin is whitish and semitransparent, so that the color of the subjacent parts gives to it a peculiar tint. The blood contained in its vessels, as is well known, is capable of modifying greatly the color of the general surface. The deep layer of the epidermis always contains more or less pigmentary matter, which gives the colors characteristic of different races, and produces the variations in complexion that are observed in different individuals of the same race. The pigment, in the white races, is but slightly developed at birth, but increases in quantity with age.

The general surface, with the exception of the palms of the hands and the soles of the feet, is covered with hairs, which are very largely developed in certain situations. The furrows and folds of the skin are produced either by the contraction of the subjacent muscles; by a loss of elasticity in the skin, as in old age; by an excessive development of fat in certain parts; or by the movements of the joints. Faint, irregular lines are observed on the surface in most parts; but upon the palms of the hands and the soles of the feet these

are well marked and regular, particularly upon the palmar surfaces of the last phalanges, where they are in the form of concentric curves, so easily observed with the naked eye that farther description is unnecessary. These lines are formed by the more or less regular arrangement of the papillæ of the true skin.

Extent and Thickness of the Skin.—Sappey has made a number of very careful observations upon the extent of the surface of the skin. Without detailing the measurements of different parts, it may be stated, as the general result of his observations, that the cutaneous surface in a good-sized man is equal to about twelve square feet; and in men of more than ordinary size it may extend to fourteen, fifteen, or even eighteen square feet. In men of medium size, in France, the surface does not exceed ten square feet; and in women, it is ordinarily from six to eight.[1] When we consider the great extent of the cutaneous surface, it is not surprising that the amount of secretion, under certain conditions, should be enormous. Indeed, under all circumstances, the amount of elimination is very considerable, and the skin is really one of the most important of the glandular structures.

The thickness of the skin varies very much in different parts. Where it is naturally exposed to constant pressure and friction, as on the soles of the feet or the palms of the hands, the epidermis becomes very much thickened, and in this way the more delicate structure of the true skin is protected. It is well known that the development of the epidermis, under these conditions, varies in different persons, with the amount of pressure and friction to which the surface is habitually subjected. The true skin is from $\frac{1}{12}$ to $\frac{1}{8}$ of an inch in thickness; but in certain parts, particularly the external auditory meatus, the lips, and the glans penis, it frequently measures not more than $\frac{1}{100}$ of an inch.[2]

[1] Sappey, *Traité d'anatomie descriptive*, Paris, 1852, tome ii., p. 447.

[2] Pouchet, *Précis d'histologie humaine*, Paris, 1864, p. 329.

Layers of the Skin.—The skin is naturally divided into two principal layers, which may be readily separated from each other by maceration. These are, the true skin (cutis vera, derma, or corium), and the epidermis, cuticle, or scarf-skin. The true skin is attached to the subjacent structures, more or less closely, by a fibrous structure called the subcutaneous areolar tissue, in the meshes of which we commonly find a certain quantity of fatty tissue. This layer is sometimes described under the name of the panniculus adiposus. The thickness of the adipose layer varies very much in different parts of the general surface and in different persons. There is no fat beneath the skin of the eyelids, the upper and outer part of the ear, the penis, and the scrotum. Beneath the skin of the cranium, the nose, the neck, and the dorsum of the hand and foot, the knee and the elbow, the fatty layer is about $\frac{1}{12}$ of an inch in thickness. In other parts it usually measures from $\frac{1}{6}$ to $\frac{1}{2}$ of an inch.[1] In very fat persons it may measure one inch or more. Upon the head and the neck, in the human subject, are muscles attached more or less closely to the skin. These are capable of moving the skin to a slight extent. Muscles of this kind are largely developed and quite extensively distributed in some of the lower animals.

There is no sharply-defined line of demarcation between the cutis and the subcutaneous areolar tissue; and the under surface of the skin is always irregular, from the presence of numerous fibres which are necessarily divided in detaching it from the subjacent structures. The fibres which enter into the composition of the skin near its under surface become looser in their arrangement, the change taking place rather abruptly, until they present large alveolæ, which generally contain a certain amount of adipose tissue.

The layer called the true skin is subdivided into a deep, reticulated, or fibrous layer, and a superficial portion, called

[1] KRAUSE, in WAGNER'S *Handwörterbuch der Physiologie*, Braunschweig, 1844, Bd. ii., S. 116.

the papillary layer. The epidermis is also divided into two layers; an external layer, called the horny layer; and an internal layer, called the Malpighian, or the mucous layer, which is in contact with the papillary layer of the corium.

The Corium, or True Skin.—The reticulated and the papillary layer of the true skin are quite distinct. The lower stratum, the reticulated, is much thicker than the papillary layer, is dense, resisting, quite elastic, and slightly contractile. It is composed of numerous bundles of white fibrous tissue interlacing with each other in every direction, generally at acute angles. Distributed throughout this layer are found numerous anastomosing elastic fibres of the small variety, and with them a number of non-striated muscular fibres. This portion of the skin contains, in addition, a considerable quantity of amorphous matter which serves to hold the fibres together. The muscular fibres are particularly abundant about the hair-follicles and the sebaceous glands connected with them, and their arrangement is such, that when they are excited to contraction by cold or by electricity, the follicles are drawn up, projecting upon the general surface, and producing the appearance known as "goose-flesh." Contraction of these fibres is particularly marked about the nipple, producing the so-called erection of this organ, and about the scrotum and penis, wrinkling the skin of these parts. The peculiar arrangement of the little muscles around the hair-follicles, forming little bands attached to the surface of the true skin and the base of the follicles, was first described by Kölliker,[1] and explains fully the manner in which the "goose-flesh" is produced. Contraction of the skin, in obedience to the stimulus of electricity, has been demonstrated by Froriep, Brown-Séquard, and Kölliker, both in the living subject and in executed criminals immediately after death.[2]

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 98.
[2] KÖLLIKER, *Manual of Human Microscopic Anatomy*, London, 1860, p. 86

The papillary layer of the skin passes insensibly into the subjacent structure and presents no well-marked line of division. It is composed chiefly of the same kind of amorphous matter that exists in the reticulated layer The papillæ themselves appear to be simply elevations of this amorphous matter, though they may contain a few fibres. In this layer we find a number of fibro-plastic nuclei with a few little corpuscular bodies called by Robin, cytoblastions.[1]

As regards their form, the papillæ may be divided into two varieties; the simple and the compound. The simple papillæ are conical, rounded, or club-shaped elevations of the amorphous matter, and are irregularly distributed on the general surface. The smallest are from $\frac{1}{700}$ to $\frac{1}{400}$ of an inch in length, and are found chiefly upon the face. The largest are on the palms of the hands, the soles of the feet, and the nipple. These measure from $\frac{1}{250}$ to $\frac{1}{200}$ of an inch. Large papillæ, regularly arranged in a longitudinal direction, are found beneath the nails. The regular, curved lines observed upon the palms of the hands and the soles of the feet, particularly the palmar surfaces of the last phalanges, are formed by double rows of compound papillæ, which present two, three, or four points attached to a single base. In the centre of each of these double rows of papillæ is an excessively fine and shallow groove, in which are found the orifices of the sudoriferous ducts.

The papillæ are abundantly supplied with blood-vessels, terminating in looped capillary plexuses, and nerves. The termination of the nerves is peculiar, and will be fully described in connection with the organs of touch. The arrangement of the lymphatics, which are very numerous in the skin, has already been indicated in the general description of the lymphatic system.[2]

[1] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Cytoblastion*.

[2] See vol. ii., Absorption, p. 430.

The Epidermis and its Appendages.—The epidermis, or external layer of the skin, is a membrane composed exclusively of cells, containing neither blood-vessels, nerves, nor lymphatics. Its external surface is marked by exceedingly shallow grooves, which correspond to the deep furrows between the papillæ of the derma. Its internal surface is applied directly to the papillary layer of the true skin, and follows closely all its inequalities. This portion of the skin is subdivided into two tolerably distinct layers. The internal layer is called the rete mucosum, or the Malpighian layer, and the external is called the horny layer. These two layers present certain important distinctive characters.

The Malpighian layer is composed of a single stratum of prismoidal, nucleated cells, containing a greater or less amount of pigmentary matter, applied directly to all the inequalities of the derma, and a number of layers of rounded cells containing no pigment. The upper layers of cells, with the scales of the horny layer, are semitransparent and nearly colorless; and it is the pigmentary layer chiefly which gives to the skin its characteristic color and the peculiarities in the complexion of different races and of different individuals. In the negro, this layer is nearly black; and when the epidermis is removed, the true skin does not present any marked difference from the skin of the white race. All the epidermic cells are somewhat colored in the dark races, but the upper layers contain no pigmentary granules. The cells of the pigmentary layer are from $\frac{1}{4000}$ to $\frac{1}{2000}$ of an inch in length, and from $\frac{1}{5000}$ to $\frac{1}{4000}$ of an inch in their short diameter. The rounded cells in the upper layers are from $\frac{1}{4000}$ to $\frac{1}{3000}$ of an inch in diameter. The absolute thickness of the rete mucosum is from $\frac{1}{1700}$ to $\frac{1}{75}$ of an inch.

The horny layer is composed of numerous strata of hard, flattened cells, irregularly-polygonal in shape, generally without nuclei, and measuring from $\frac{1}{2000}$ to $\frac{1}{750}$ of an inch in diameter. The deeper cells are thicker and more rounded than those of the superficial layers.

The epidermis serves as a protection to the more delicate structure of the true skin, and its thickness is proportionate to the exposure of the different parts. It is consequently much thicker upon the soles of the feet and the palms of the hands than in other portions of the general surface, and its thickness is very much increased in those who are habitually engaged in severe manual labor. Upon the face, the eyelids, and in the external auditory passages, the epidermis is most delicate, measuring from $\frac{1}{900}$ to $\frac{1}{600}$ of an inch in thickness. Upon the palm it is from $\frac{1}{36}$ to $\frac{1}{24}$ of an inch thick, and upon the sole of the foot it measures from $\frac{1}{16}$ to $\frac{1}{5}$ of an inch.[1] These variations depend entirely upon the development of the horny layer. The thickness of the rete mucosum, although it presents considerable variation in different parts, is rather more uniform.

There is constantly more or less desquamation of the epidermis, particularly the horny layer, and the cells are regenerated by a blastema exuded from the subjacent vascular parts. It is probable that there is a constant formation of cells in the deeper strata of the horny layer, which become flattened as they near the surface; but there is no direct evidence that the cells of the rete mucosum undergo transformation into the hard, flattened scales of the horny layer.

Physiological Anatomy and Uses of the Nails and Hairs.—It is unnecessary, in this connection, to discuss very minutely the anatomy of the nails and hairs. They are ordinarily regarded as appendages of the epidermis, produced by certain peculiar organs belonging to the true skin; and an elaborate study of these parts belongs strictly to descriptive and general anatomy. To complete, however, the physiological history of the skin, it will be necessary to

[1] Kölliker, *Manual of Human Microscopical Anatomy*, American Edition, Philadelphia, 1854, p. 146. Kölliker gives (*loc. cit.*) accurate measurements of the epidermis in many different portions of the skin, to which the reader is referred for farther information on this point.

consider briefly the general arrangement of the cuticular appendages.

The nails are situated on the dorsal surfaces of the distal phalanges of the fingers and toes. They serve to protect these parts, and in the fingers, are also quite important in prehension. The general appearance of the nails is so familiar that it requires no special description. In their study, anatomists have distinguished a root, a body, and a free border.

The root is thin and soft, terminating in rather a jagged edge, which is turned slightly upward and is received into a fold of the skin extending around the nail to its free edge. The length of the root of course varies with the size of the nail, but it is generally from one fourth to one third of the length of the body.

The body of the nail extends from the fold of skin which covers the root to the free border. This portion of the nail, with the root, is closely adherent by its under surface to the true skin. It is marked by fine but distinct longitudinal striæ and very faint transverse lines. It is usually reddish in color, from the great vascularity of the subjacent structure. At the posterior part is a whitish portion of a semilunar shape, called the lunula, which has this appearance simply from the fact that the corium in this part is less vascular, and the papillæ are not so regular as in the rest of the body. That portion of the skin situated beneath the root and the body of the nail is called the matrix. It presents highly vascular papillæ, arranged in regular, longitudinal rows, and receives into its grooves corresponding ridges on the under surface of the nail.

The free border of the nail begins at the point where the nail becomes detached from the skin. This is generally cut or worn away, and is constantly growing; but if left to itself, it attains in time a definite length, which may be stated, in general terms, to be from an inch and a half to two inches.

Examining the nail in a longitudinal section, the horny

layer, which is usually regarded as the true nail, is found to increase progressively in thickness from the root to near the free border. If the nail be examined in a transverse section, it will also be found much thicker in the central portion than near the edge, and that part which is received into the lateral portions of the fold becomes excessively thin like the rest of the root. The thickness of the true nail at the root is from $\frac{1}{200}$ to $\frac{1}{100}$ of an inch; and, in the thickest portion of the body, it usually measures from $\frac{1}{40}$ to $\frac{1}{30}$ of an inch. The nail becomes somewhat thinner at and near the free border.

Sections of the nails show that they are composed of two layers, which correspond to the Malpighian and the horny layer of the epidermis, though they are much more distinct. The Malpighian layer is applied directly to the ridges of the bed of the nail, and presents upon its upper surface ridges much less strongly marked than in the underlying true skin. This layer is rather thinner than the horny layer, is whitish in color, and is composed of numerous strata of elongated, prismoidal, nucleated cells, arranged perpendicularly to the matrix. These cells are from $\frac{1}{3000}$ to $\frac{1}{1700}$ of an inch in length.

The horny layer, which constitutes the true nail, is applied by its under surface directly to the ridges of the Malpighian layer. It is dense and brittle, and composed of numerous strata of flattened cells, which cannot be isolated without the use of reagents. If the different strata of this portion of the nail be studied after boiling in a dilute solution of soda or potash, it becomes evident that here, as in the horny layer of the epidermis, the lower cells are somewhat rounded, while those nearer the surface are flattened. These cells are nearly all nucleated, and measure from $\frac{1}{1000}$ to $\frac{1}{750}$ of an inch in diameter. The thickness of this layer varies in different portions of the nail, while the Malpighian layer is nearly uniform. This layer is constantly growing, and constitutes the entire substance of the free borders of the nails.

The connections of the nails with the true skin resemble those of the epidermis; but the relations of these structures to the epidermis itself are somewhat peculiar. Up to the fourth month of fœtal life, the epidermis covering the dorsal surfaces of the last phalanges of the fingers and toes does not present any marked peculiarities; but at about the fourth month, the peculiar hard cells of the horny layer of the nails make their appearance between the Malpighian and the horny layer of the epidermis, and at the same time the Malpighian layer beneath this plate, which is destined to become the Malpighian layer of the nails, is somewhat thickened, and the cells assume more of an elongated form. The horny layer of the nails constantly thickens from this time; but until the end of the fifth month, it is covered by the horny layer of the epidermis. After the fifth month, the epidermis breaks away and disappears from the surface; and at the seventh month, the nails begin to increase in length. Thus, at one time, the nails are actually included between the two layers of the epidermis; but after they have become developed, they are simply covered at their roots by a narrow border of the horny layer, the epidermis commencing again under the nail where the free border leaves the bed. The nails are therefore to be regarded as modifications of the horny layer of the epidermis, possessing certain anatomical and chemical peculiarities. The Malpighian layer of the nails is continuous with the same layer of the epidermis, but the horny layers are, as we have seen, distinct.

One of the most striking peculiarities of the nails is in their mode of growth. The Malpighian layer is stationary, but the horny layer is constantly growing, if the nails be cut, from the root and bed. It is evident that the nails grow from the bed, as their thickness progressively increases in the body from the root to near the free border; but their longitudinal growth is by far the more rapid. Indeed, the nails are constantly pushing forward, increasing in thickness

as they advance. Near the end of the body, as the horny layer becomes thinner, the growth from below is diminished

Hairs, varying greatly in size and development, cover nearly every portion of the surface of the body. The only parts in which they are not found are the palms of the hands and soles of the feet, the palmar surface of the fingers and toes, the dorsal surface of the last phalanges of the fingers and toes, the lips, the upper eyelids, the lining of the prepuce, and the glans penis. Some of the hairs are long, others are short and stiff, and others are fine and downy. These differences have led to a division of the hairs into three varieties.

The first variety includes the long, soft hairs, which are found on the head, on the face in the adult male, around the genital organs and under the arms in both the male and the female, and sometimes upon the breast and over the general surface of the body and extremities, particularly in the male.

The second variety, the short, stiff hairs, is found at the entrance of the nostrils, upon the edges of the eyelids, and upon the eyebrows.

The third variety, the short, soft, downy hairs, are found on the general surface not occupied by the long hairs, and the caruncula lachrymalis. In early life, and ordinarily in the female at all ages, the trunk and extremities are covered with downy hairs; but in the adult male, these frequently become developed into long, soft hairs.

The hairs are usually set obliquely in the skin, and take a definite direction as they lie upon the surface. Upon the head and face, and, indeed, the entire surface of the body, the general course of the hairs may be followed out, and they present currents or sweeps that have nearly always the same direction. These "currents" have been carefully studied by Wilson, and are fully described in his work upon the healthy skin.[1]

[1] WILSON, *Healthy Skin*, Philadelphia, 1854, p. 101, *et seq.*

The diameter and length of the hairs are exceedingly variable in different persons, especially in the long, soft hairs of the head and beard. It may be stated in general terms that the long hairs attain the length of from twenty inches to three feet in women, and considerably less in men. There are instances, however, in women, in which the hair of the head measures considerably more than three feet, but these are quite unusual. Like the nails, the hair, when left to itself, attains in three or four years a definite length, but when it is habitually cut it grows constantly. The short, stiff hairs are from one quarter to one half an inch in length. The soft, downy hairs measure ordinarily from one twelfth to one half an inch. Hairs that have never been cut terminate in pointed extremities; and sometimes in hairs that have been cut, the ends become somewhat pointed, though they are never so sharp as in the new hairs.

Of the long hairs, the finest are upon the head, where they average about $\frac{1}{400}$ of an inch in diameter, the extremes ordinarily being from $\frac{1}{1500}$ to $\frac{1}{500}$ of an inch for the finest, and from $\frac{1}{400}$ to $\frac{1}{140}$ of an inch for the coarsest. The hair is ordinarily coarser in women than in men. Dark hair is ordinarily coarser than light hair; and upon the same head the extremes of variation are sometimes observed.[1] The hairs of the beard and the long hairs of the body are coarser than the hairs of the head. Wilson estimates that the average number of hairs upon a square inch of the scalp is about 1,000, and the number upon the entire head about 120,000.

The short, stiff hairs are from $\frac{1}{400}$ to $\frac{1}{170}$ of an inch in diameter, and the fine, downy hairs from $\frac{1}{2000}$ to $\frac{1}{1200}$ of an inch. The variations in the color of the hairs in different races and in different individuals of the same race are sufficiently familiar.

When the hairs are in a perfectly normal condition, they are very elastic, and may be stretched to from one fifth to one third more than their original length. Their strength

[1] WILSON, *op. cit.*, p. 84, *et seq.*

varies with their thickness, but an ordinary hair from the head will bear a weight of six or seven ounces. A well-known property of the hair is that of becoming strongly electric by friction; and this is particularly well-marked when the weather is cold and dry. The electricity thus excited is negative. Sections of the shaft of the hairs show that they are oval, but their shape is very variable, straight hairs being nearly round, while curled hairs are quite flat. Another peculiarity of the hairs is that they are strongly hygrometric. They readily absorb moisture and become sensibly elongated, a property which has been made use of by physicists in the construction of delicate hygrometers.

Roots of the Hairs and Hair-follicles.—The roots of the hairs are embedded in follicular openings in the skin, which differ in the different varieties only in the depth to which they penetrate the cutaneous structure. In the downy hairs, the roots pass only into the superficial layers of the true skin; but in the thicker hairs, the roots pass through the skin and penetrate the subcutaneous cellulo-adipose tissue.

The root of the hair is softer, rounder, and a little larger than the shaft. It becomes enlarged into a rounded bulb at the bottom of the follicle, and rests upon a fungiform papilla, constricted at its base, to which it is closely attached. In describing the connection between the hairs and the skin, anatomists mention three membranes forming the walls of the hair-follicles, and two membranes that envelop the roots of the hair in the form of a sheath. The study of these parts is much simplified by keeping constantly in view the correspondence between the different layers of the follicles and the layers of the true skin, and the relations of the root-sheaths with the epidermis.

The follicles are tubular inversions of the structures that compose the corium, and their walls present three distinct membranes. Their length is from $\frac{1}{12}$ to $\frac{1}{4}$ of an inch. The membrane that forms their external coat is composed of

inelastic fibres arranged for the most part longitudinally, provided with blood-vessels and a few nerves, containing some fibro-plastic elements, but deprived entirely of elastic tissue. This is the thickest of the three membranes and is closely connected with the corium. Next to this is a fibrous membrane composed of fusiform, nucleated fibres arranged transversely. These resemble the organic muscular fibres, but are believed by Kölliker to be fibres of connective tissue.[1] The internal membrane is structureless, and corresponds to the amorphous layer of the true skin. The papilla at the bottom of the hair-sac varies in size with the size of the hairs, and is connected with the fibrous layers of the walls of the follicle. It is composed of amorphous matter with a few granules and nuclei, and probably contains blood-vessels and nerves, though these are not very distinct.

Although these different membranes are sufficiently recognizable, it is evident that the hair-sac is nothing more than an inversion of the corium, with some slight modifications in the character and arrangement of its anatomical elements. The fibrous membranes correspond to the deeper layers of the true skin, wanting the elastic elements, and presenting a peculiar arrangement of its inelastic fibres, the external fibres being longitudinal and the internal fibres transverse. The structureless membrane corresponds to the upper layers of the true skin, which are composed chiefly of amorphous matter. The hair-papilla corresponds to the papillæ on the general surface of the corium.

The investment of the root of the hair presents two distinct layers. The external root-sheath is three or four times as thick as the inner membrane, and corresponds exactly with the Malpighian layer of the epidermis. This sheath is continuous with the bulb of the hair. The internal root-sheath is a transparent membrane, composed of flattened cells, mostly without nuclei. This extends from the bottom of the hair-follicle, and covers the lower two-thirds of the root.

[1] Kölliker, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 132.

Summary.—The essential points in the anatomy of the hair-follicles and the connections of the hairs with the skin may be summed up in a few words:

Fig. 5.

Hair and hair-follicle of medium size, magnified fifty diameters—*a*, shaft of the hair; *b*, root; *c*, bulb, *d*, epidermis of the hair; *e*, internal root-sheath; *f*, external sheath; *g*, amorphous membrane of the follicle; *h*, layers of transverse and longitudinal fibres; *i*, papilla; *k*, excretory ducts of the sebaceous glands; *l*, derma at the point of opening of the follicle; *m*, mucous layer of the epidermis; *n*, horny layer of the epidermis; *o*, termination of the internal sheath of the root of the hair. (KÖLLIKER, *Éléments d'histologie humaine*, Paris, 1868, p. 165.)

The hair-follicle consists of an inversion of the true skin, with some modifications in the arrangement of its anatomical elements, and presents at the bottom an ovate papilla, upon which the bulb of the hair rests and to which it is closely attached. The root of the hair is invested with two membranes; the outer sheath corresponding to the Malpighian layer of the epidermis, and the inner sheath corresponding to the horny layer. These membranes, with the membranes that form the wall of the follicle, extend to the junction of the lower two-thirds with the upper third of the follicle, or the openings of the sebaceous glands, with which all the hairs are provided. If continued upon the skin, of course the layers would be reversed, the inner root-sheath becoming the outer layer of the epidermis, the outer root-sheath being continuous with the Malpighian layer. The hair itself is an appendage of the epidermis, and is continuous with the inner root-sheath, which corresponds to the Malpighian layer. It rests upon and is produced by the papilla, as the nail rests upon the papillæ of its matrix. The root of

the hair and the structure of its sheaths and the hair-follicle are shown in Fig. 5.

Structure of the Hairs.—The different varieties of hairs present certain peculiarities in their anatomy, but all of them are composed of a fibrous structure forming the greater part of their substance, covered by a thin layer of imbricated cells. In the short, stiff hairs, and in the long, white hairs, there is a distinct medullary substance; but this is wanting in the downy hairs, and is indistinct in many of the long, dark hairs.

The fibrous substance is composed of hard, elongated, longitudinal fibres, which cannot be isolated without the aid of reagents. They may be separated, however, by treating with warm sulphuric acid, when they present themselves in the form of dark, irregular, spindle-shaped plates, from $\frac{1}{500}$ to $\frac{1}{350}$ of an inch long, and from $\frac{1}{6000}$ to $\frac{1}{3000}$ of an inch wide. These contain pigmentary matter of various shades, occasional cavities filled with air, and a few nuclei. The pigment may be of any color, from a light yellow to an intense black, and it is this substance that gives to the hair the great variety in color which is observed in different persons. In the lower part of the root the fibres are much shorter, and at the bulb become transformed, as it were, into the soft, rounded cells found in this situation covering the papilla.

The epidermis of the hair is excessively thin, and is composed of flattened, quadrangular plates, overlying each other from below upward. These scales, or plates, are without nuclei, and exist in a single layer over the shaft of the hair and the upper part of its root; but in the lower part of the root the cells are thicker, softer, are frequently nucleated, and exist in two layers.

The medulla is found in the short, stiff hairs, and it is often beautifully distinct in the long, white hairs of the head. According to Sappey, it is found more or less distinctly

marked in all the long hairs, as is seen on transverse section.[1] It forms from one-sixth to one-third of the diameter of the hair. The medulla can be traced, under favorable circumstances, from just above the bulb to near the pointed extremity of the hairs. It is composed of small, rounded cells, from $\frac{1}{1500}$ to $\frac{1}{1200}$ of an inch in diameter, nucleated, and frequently containing dark granules of pigmentary matter. Mixed with these cells are numerous air-globules; and frequently the cells are interrupted for a short distance and the space is occupied with air. The dark granules of the medullary cells are supposed by Kölliker to be merely globules of air.[2] The medulla likewise contains a glutinous fluid between the cells and surrounding the air-globules.

Growth of the Hairs.—Although not provided with blood and deprived of sensibility, the hairs are connected with vascular parts and are regularly nourished by imbibition from the papillæ. Each hair is first developed in a closed sac, and at about the sixth month its pointed extremity perforates the epidermis. These first-formed hairs are afterward shed, like the milk teeth, being pushed out, as it were, by new hairs from below, which arise from a second and more deeply-seated papilla. This shedding of the hairs, which was first described by Kölliker,[3] usually takes place from two to six months after birth.

The difference in the color of the hair depends upon differences in the quantity and the tint of the pigmentary matter; and in old age, the hair becomes white or gray from a blanching of the cortex and medulla.

Sudden Blanching of the Hair.—It is an interesting question, in connection with the nutrition of the hair, to examine the instances so often quoted of sudden blanching of the hair from violent emotions or other causes. Some

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1852, tome ii., p. 500.

[2] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 130.

[3] *Op. cit.*, S. 137.

physiologists are of the opinion that the hair may become almost white in the course of a few hours, and this, indeed, is a popular impression; but others assume that such sudden changes never take place, although it is certain that the hair frequently turns gray in a few weeks. In examining the literature of this subject, it is difficult to find in the older works well-authenticated cases of these sudden changes, and most of those that have been quoted are taken upon the loose authority of persons evidently not in the habit of making scientific observations. Such instances, unsupported by analogous cases of a reliable character, must necessarily be rejected, as not fulfilling the rigid requirements demanded in scientific inquiries, in which all possible sources of error should be carefully excluded. It is not necessary, therefore, to quote the instances of sudden blanching of the hair recorded by the ancient writers, nor those well-known cases of later date, so often detailed in scientific works, such as that of Marie Antoinette or Sir Thomas More; and it seems proper to exclude, also, cases in which the blanching of the hair has been observed only by friends or relatives; for in most of them the statements with regard to time are conflicting and unsatisfactory.

Regarding the subject, however, from a purely scientific point of view, there are a few instances of late date, in which sudden blanching of the hair has been observed, and the causes of this remarkable phenomenon fully investigated by competent observers; and it is almost unnecessary to say that a single well-authenticated case of this kind demonstrates the possibility of its occurrence, and is interesting in connection with the reported instances which have not been subjected to proper investigation. One of these cases is reported in *Virchow's Archiv*, for April, 1866, by Dr. Landois, as occurring under the observation of himself and Dr. Lohmer.[1] In this case the blanching of the hair occurred in a hospital

[1] LANDOIS, *Das plötzliche Ergrauen der Haupthaare.*—VIRCHOW'S *Archiv*, Berlin, 1866, Bd. xxxv., S. 375.

in a single night, while the patient was under the daily observation of the visiting physician. As this is one of the few well-authenticated instances of sudden blanching of the hair, we shall give, in a few words, its essential particulars:

The patient, a compositor, thirty-four years of age, with light hair and blue eyes, was admitted into the hospital, July 9, 1865, suffering apparently from an acute attack of delirium tremens. A marked peculiarity in the disease was excessive terror when any person approached the patient. He slept for twelve hours on the night of the eleventh of July, after taking thirty drops of laudanum. Up to this time nothing unusual had been observed with regard to the hair. On the morning of July 12th, it was evident to the medical attendants and all who saw the patient that the hair of the head and beard had become gray. This fact was also remarked by the friends who visited the patient, and he himself called for a mirror, and remarked the change with intense astonishment. The patient continued in the hospital until September 7th, when he was discharged, the hair remaining gray.

An interesting point connected with this case is the fact that the hairs were submitted to careful microscopical examination. The white hairs were found to contain a great number of air-globules in the medulla and in the cortical substance, but the pigment was everywhere preserved. The presence of air gave the hairs a dark appearance by transmitted light and a white appearance by reflected light. Dr. Landois quotes, in this connection, instances of blanching of the hair, in which each hair presented alternate rings of a white and brown color. Another very curious case of this kind was lately reported to the Royal Society by Mr. Erasmus Wilson.[1] In this case, the white portions presented, on a microscopical examination, great bubbles of air;

[1] WILSON, *On a remarkable Alteration of Appearance and Structure of the Human Hair.—Proceedings of the Royal Society*, London, 1867, vol. xv., No. 91, p. 406, *et seq.*

but there was no diminution in the quantity of pigmentary matter. The possibility of sudden blanching of the hair is farther illustrated by a curious observation lately made by Dr. Brown-Séquard. This physiologist observed in his own person four white hairs upon the cheeks upon one side, and seven upon the other, mixed with the dark hairs of the beard. These he pulled out, and two days after, he found two hairs upon one side, and three upon the other, that were white throughout their entire length. This observation he verified several times, and from this he concludes that there is no doubt of the "possibility of a very rapid transformation (probably in less than one night) of black hairs into white."[1]

The microscopical examinations by Dr. Landois and others leave no doubt as to the cause of the white color of the hair in cases of sudden blanching; and the instances we have just quoted show that the fact of the occurrence of this phenomenon can no longer be called in question. All are agreed that there is no diminution in the pigment, but that the greater part of the medulla becomes filled with air, small globules being also found in the cortical substance. The hair in these cases presents a marked contrast with hair that has become gray gradually from old age, when there is always a loss of pigment in the cortex and medulla. How the air finds its way into the hair in sudden blanching it is difficult to imagine; and the views that have been expressed on this subject by different authors are entirely theoretical.

The fact that the hair may become white or gray in the course of a few hours renders it probable that many of the cases reported upon unscientific authority actually occurred; and these have all been supposed to be connected with intense grief or terror. The terror was very marked in the case reported by Dr. Landois. In the great majority of

[1] Brown-Séquard, *Expériences démontrant que les poils peuvent passer rapidement de noir au blanc, chez l'homme.*—*Archives de physiologie*, Paris, 1869, tome ii., p. 442.

recorded observations, the sudden blanching of the hair has been apparently connected with intense mental emotion; but this is all that can be said on the subject of causation, and the mechanism of the change is not understood.

Uses of the Hairs.—The hairs serve an important purpose in the protection of the general surface and in guarding certain of the orifices of the body. The hair upon the head and the face protects from cold and shields the head from the rays of the sun during exposure in hot climates. Although the amount of hair upon the general surface is small, as it is a very bad conductor of caloric, it serves in a degree to maintain the heat of the body. It also moderates the friction upon the surface. The eyebrows prevent the perspiration from running from the forehead upon the lids; the eyelashes protect the surface of the conjunctiva from dust and other foreign matters; the mustache protects the lungs from dust, a function very important to those exposed to dust in long journeys or in their daily work; the short, stiff hairs at the openings of the ears and nose protect these orifices. It is difficult to assign any special office to the hairs in some other situations, but their general uses are sufficiently evident.

Perspiration.

In the fullest acceptation of the term, perspiration embraces the entire function of the skin as an excreting organ, and includes the exhalation of carbonic acid as well as of watery vapor and organic matter. The office of the skin as an eliminator is undoubtedly very important; but the quantity of excrementitious matters with the properties of which we are well acquainted, such as carbonic acid and urea, thrown off from the general surface, is small as compared to the amount exhaled by the lungs and kidneys. If the surface of the body be covered with an impermeable coating, death always takes place; but the phenomena which precede the fatal result are difficult to explain. The experiments on this

subject by Fourcault,[1] Bouley and Bernard,[2] and others, are very interesting. In these observations, cutaneous exhalation was entirely suppressed in horses, rabbits, and other animals, by covering the surface with an impermeable coating of varnish or pitch; and the animals died at periods varying from a few hours to ten days, the gravity of the symptoms depending upon the thoroughness with which the coating had been applied. The experiments of Bernard, particularly, were most curious and interesting. He confirmed the observations of Fourcault and Bouley on the effects of covering the entire surface, in horses, with an impermeable coating, but he found that when a space of even a few inches was left uncovered, the animals survived; and in animals that were suffering from the effects of a complete coating, if a small portion were removed, the symptoms were ameliorated and recovery took place.[3] These experiments led Bernard to the conclusion that death does not take place, after complete suppression of the functions of the skin, from retention of carbonic acid alone.

One of the well-known objects of cutaneous exhalation is to keep down the animal temperature by evaporation, when there is a tendency to too great development of heat by exercise or from other causes; and it might be supposed that the suppression of this function would be one of the chief causes of the fatal result. It is curious, however, that in the early experiments of Fourcault,[4] and in the later observations of Bernard, the animals suffered a great diminution in temperature. Bernard found that death occurred when the temperature was between 68° and 72° Fahr., always

[1] FOURCAULT, *Expériences démontrant l'influence de la suppression méchanique de la transpiration cutanée sur l'altération du sang.—Comptes rendus*, Paris, 1838, tome vi., p. 369, and Ibid., 1843, tome xvi., p. 139.

[2] BERNARD, *Leçons sur les propriétés, etc., des liquides de l'organisme*, Paris, 1859, tome ii., p. 177.

[3] *Op. cit.*, p. 178.

[4] FOURCAULT, *loc. cit.*

taking place more rapidly when the surrounding temperature was lowered.[1]

In some later observations upon this subject by Valentin and Laschkewitsch, facts, still more curious, have been developed. Laschkewitsch[2] found that the peculiar effects of an impermeable coating to the surface were much less marked in large than in small animals. Horses treated in this way lived for several days, but rabbits died in a few hours. In rabbits, death frequently occurred after coating only one quarter of the surface. Valentin and Laschkewitsch confirmed the observations on the lowering of the animal temperature; but they found that when the heat was kept at the normal standard by artificial means, no morbid symptoms were manifested. Neither of these observers could detect any accumulation of excrementitious or other morbid principles in the blood; and the results of their experiments were opposed to the view that death takes place, under these conditions, from asphyxia. The cause of death has never, indeed, been satisfactorily explained, partly for the reason that we are unacquainted with the nature and properties of all the excrementitious matters exhaled from the skin; and it is not easy to understand why coating the surface should be followed by such a rapid diminution in the temperature of the body. The experimental facts, however, would indicate that the skin possesses important functions with which we are entirely unacquainted. Physiological chemists have detected urea and some other effete matters in the perspiration, but it is probable that some volatile principles are eliminated by the general surface, which have thus far escaped observation. The importance of free action of the skin in the human subject was strikingly illustrated in the case of a child who was covered with gold-leaf in

[1] BERNARD, *op. cit.*, p. 177.

[2] LASCHKEWITSCH, *Ueber die Ursachen der Temperatur-Erniedrigung bei Unterdrükung der Hautperspiration.—Archiv für Anatomie, Physiologie, und wissenschaftliche Medicin*, Leipzig, 1868, No. i., S. 61, *et seq.*

order to represent an angel in the ceremonies attending the coronation of Pope Leo X. This child died a few hours after the coating had been applied.[1]

Sudoriparous Glands.—The most numerous and the most important glands of the skin are those which secrete the perspiration. The other glands, which have been already considered, have rather a mechanical function, serving to keep the skin and its appendages in a proper condition for the protection of the subjacent parts; but it is the perspiratory apparatus alone which is concerned in the great function of elimination.

With few exceptions, every portion of the skin is provided with sudoriparous glands. They are not found, however, in the skin covering the concave surface of the concha of the ear, the glans penis, the inner lamella of the prepuce, and, unless the ceruminous glands be regarded as sudoriparous organs, the external auditory meatus. Kölliker states that some other portions of the skin are deprived of sweat-glands, but he does not indicate their situation.[2]

On examining the surface of the skin with a low magnifying power, especially on the palms of the hands and the soles of the feet, the orifices of the sudoriferous ducts may be seen in the middle of the papillary ridges, forming a regular line in the shallow groove between the two rows of papillæ. The tubes always open upon the surface obliquely. If a thin section of the skin be carefully made and examined microscopically, the ducts are seen passing through the different layers and terminating in rounded, convoluted coils in the subcutaneous structure. These little rounded, or ovoid bodies, which constitute the sudoriparous, or sweat-producing apparatus, may be seen attached to the under surface of the skin, when it is removed from the subjacent parts by maceration. The perspiratory apparatus consists,

[1] Laschkewitsch, *loc. cit.*

[2] Kölliker, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 139

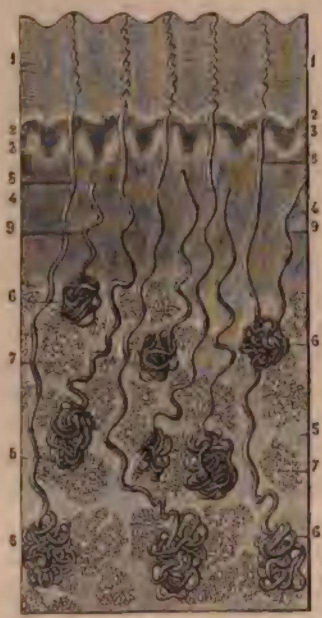
indeed, of a simple tube, presenting a coiled mass beneath the skin, the sudoriparous portion, and a tube of greater or less length, in proportion to the thickness of the cutaneous layers, which is the excretory duct, or the sudoriferous portion.

The glandular coils vary in size from $\frac{1}{125}$ to $\frac{1}{25}$ of an inch; the smallest coils being found beneath the skin of the penis, the scrotum, the eyelids, the nose, and the convex surface of the concha of the ear, and the largest on the areola of the nipple and the perineum. Very large glands are found mixed with smaller ones in the axilla, but these produce a peculiar secretion which will be specially considered. The coiled portion of the tube is about $\frac{1}{350}$ of an inch in diameter, and forms from six to twelve convolutions. It consists of a sharply defined, strong, external membrane, from $\frac{1}{6000}$ to $\frac{1}{3500}$ of an inch in thickness, very transparent, uniformly granular, and sometimes indistinctly striated. This is of uniform diameter throughout the coil, and terminates in a very slightly dilated, rounded, blind extremity. It is filled with epithelium in the form of finely granular matter, usually not segmented into cells, and provided with small oval nuclei. The glandular mass is surrounded with a plexus of capillary blood-vessels, which send a few small branches between the convolutions of the coil. Sometimes the coil is enclosed in a delicate fibrous envelope.

The excretory duct is simply a continuation of the glandular coil. Its course through the layers of the true skin is nearly straight. It then passes into the epidermis between the papillæ of the corium, and presents, in this layer, a number of spiral turns. The spirals vary in number according to the thickness of the epidermis. Sappey has found from six to ten in the palms of the hands, and from twelve to fifteen in the soles of the feet. As it emerges from the glandular coil, the excretory duct is somewhat narrower than the tube in the secreting portion; but as it passes through the epidermis, it again becomes larger. It possesses the same

external membrane as the glandular coil, and is lined generally by two layers of cells of pavement-epithelium.[1]

FIG. 6.



Sudoriparous glands, magnified twenty diameters. 1, 1, Epidermis; 2, 2, mucous layer; 3, 3, papillæ; 4, 4, derma; 5, 5, subcutaneous areolar tissue; 6, 6, 6, 6, sudoriparous glands; 7, 7, adipose vesicles; 8, 8, excretory ducts in the derma; 9, 9, excretory ducts divided. (SAPPEY, *Traité d'anatomie*, Paris, 1852, tome ii., p. 466.)

In a section of the skin and the subcutaneous tissue, involving several of the sudoriparous glands with their ducts, it is seen that the glandular coils are generally situated at different planes beneath the skin, as is indicated in Fig. 6.

Robin has described a variety of sudoriparous glands in the axilla, which do not differ so much from the glands in other parts in their anatomy, as in the character of their secretion.[2] The coil in these glands is much larger than in other parts, measuring from $\frac{1}{25}$ to $\frac{1}{12}$ of an inch; the walls of the tube are thicker, and present an investment of fibrous tissue with an internal layer of longitudinal, unstriped muscular fibres;[3] and finally, the tubes of the coil itself are lined with cells of pavement-epithelium. They are very numerous in the axilla, forming a continuous layer beneath the skin. Mixed with these glands are a few of the ordinary variety.

Estimates have been made by different writers of the absolute number of sudoriparous glands in the body, and

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1852, tome ii., p. 468.

[2] ROBIN, *Note sur une espèce particulière de glandes de la peau de l'homme.—Annales des sciences naturelles, Zoologie*, 3me série, Paris, 1845, p. 380.

[3] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 140.

the probable extent of the exhalant surface of the skin. One of the most careful, and probably the most reliable of these estimates, is that made by Krause; but like all estimates of this kind, the results are to be taken as merely approximative. Krause found great differences in the number of perspiratory openings in different portions of the skin, and estimated the number in a square inch in certain parts, as follows: On the forehead, he found 1,258 glands to a square inch; on the cheeks, 548; on the anterior and lateral portions of the neck, 1,303; on the breast and abdomen, 1,136; on the back of the neck, the back, and the nates, 417; the forearm, inner surface, 1,123, and the outer surface, 1,093; on the hand, palmar surface, 2,736, and dorsal surface, 1,490; on the upper part of the thigh, inner surface, 576, outer surface, 554; on the lower part of the thigh, inner surface, 576; on the foot, plantar surface, 2,685, and the dorsal surface, 924.[1] From these figures it is estimated that the entire number of perspiratory glands is 2,381,248; and assuming that each coil when unravelled measures about $\frac{1}{16}$ of an inch, the entire length of the secreting tubes is about $2\frac{1}{2}$ miles. It must be remembered, however, that the length of the secreting coil only is given, and that the excretory ducts are not included.[2]

Mechanism of the Secretion of Sweat.—The action of the skin as a glandular organ is continuous and not intermittent; but under ordinary conditions, the sweat is exhaled from the general surface in the form of vapor. With regard

[1] KRAUSE, *Haut*, in WAGNER, *Handwörterbuch der Physiologie*, Braunschweig, 1844, Bd. ii., S. 131.

[2] If the above calculation be approximatively correct, the estimate given by Wilson, which is frequently quoted in works on physiology, must be very much exaggerated. Wilson assumes that the average number of pores to the square inch of surface is 2,800; and, including the length of excretory duct, he estimates that each tube measures about a quarter of an inch. Assuming that the number of square inches of surface is 2,500 (a little more than the estimate of Haller, which is fifteen square feet) it is estimated that the total length

to the mechanism of its separation from the blood, nothing is to be said in addition to the general remarks upon the subject of secretion; and it is probable that the epithelium of the secreting coils is the active agent in the selection of the peculiar matters which enter into its composition. There are no examples of the separation by glandular organs of vapor from the blood, and the perspiration is secreted as a liquid, and only becomes vaporous as it is discharged upon the surface.

The influence of the nervous system upon this secretion is remarkable. It is well known, for example, that an abundant production of perspiration is frequently the result of mental emotions. Bernard has shown, in a series of interesting experiments, that the nervous influence may be propagated through the sympathetic system. In one of these observations, he divided the sympathetic in the neck of a horse, producing, as a consequence, an elevation in temperature and increase in the arterial pressure in the part supplied with branches of the nerve. He found, also, that the skin of the part became covered with a copious perspiration. Upon galvanizing the divided extremity of the nerve, the secretion of sweat was arrested.[1] When the skin is in a normal condition, after exercise or whenever there is a tendency to elevation of the animal temperature, there is a determination of blood to the surface, accompanied with an increase in the secretion of sweat. This is the case when the body is exposed to a high temperature; and it is by an increase in the transpiration from the surface that the animal heat is maintained at the normal standard.

Quantity of Cutaneous Exhalation.—The amount of cutaneous exhalation is subject to great variations, depend-

of perspiratory tubing is nearly twenty-eight miles. In a note, however, it is stated that the sebiparous system is included in this calculation (ERASMUS WILSON, *Healthy Skin*, Philadelphia, 1854, p. 63).

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 183.

ing upon conditions of temperature and moisture, exercise, the quantity and character of the ingesta, etc. Most of these variations relate to the function of the skin in regulating the temperature of the body; and it is probable that the elimination of excrementitious matters by the skin is not subject, under normal conditions, to the same modifications, although positive experiments upon this point are wanting. It is not designed, in this connection, to discuss all the experiments that have been made upon the quantity and the modifications of the cutaneous exhalations, and we will only consider what appear to be the most reliable of the numerous recorded observations upon this subject. The classical experiments of Sanctorius were among the first attempts to determine by the balance the relations of the ingesta to the exhalations;[1] but these were necessarily imperfect, on account of the difficulty in constructing proper instruments for the investigations, and the cutaneous and pulmonary exhalations were estimated together. When there is such a wide range of variation in different individuals and in the same person under different conditions of season, climate, etc., it is only possible to give approximate estimates of the quantity of sweat secreted and exhaled in the twenty-four hours; and more recent observations have shown that the calculations of Seguin and Lavoisier,[2] made in 1790, are as nearly correct as possible. These observers estimated the daily quantity of cutaneous transpiration at about two pounds (one pound and fourteen ounces). The estimates of Krause[3] and of Valentin[4] are a little less, but the difference is not considerable.

[1] SANCTORIUS, *Medicina Statica:* by JOHN QUINCY, M. D., London, 1723, p. 48, *et seq.*

[2] SEGUIN ET LAVOISIER, *Premier mémoire sur la transpiration des animaux.—Histoire de l'Académie des Sciences, année*, 1790, Paris, 1797, p. 609.

[3] KRAUSE, *Haut*, in WAGNER, *Handwörterbuch der Physiologie*, Braunschweig, 1844, Bd. ii., S. 139, *et seq.*

[4] VALENTIN, *Lehrbuch der Physiologie des Menschen*, Braunschweig, 1844, Bd. i., S. 714, *et seq.*

Under violent and prolonged exercise, the loss of weight by exhalation from the skin and lungs may become very considerable. It is stated by Mr. Maclaren, the author of an excellent work on training, that in one hour's energetic fencing, the loss by perspiration and respiration, taking the average of six consecutive days, was about three pounds, or accurately, forty ounces, with a varying range of eight ounces.[1]

When the body is exposed to a very high temperature, the amount of exhalation from the surface is immensely increased; and it is by this rapid evaporation that persons have been able to endure for several minutes a temperature considerably exceeding that of boiling water. Dr. Southwood Smith made some very interesting observations on this point upon workmen employed about the furnaces of gas-works and exposed to intense heat; and he found that in an hour, the loss of weight amounted to from two to four pounds, this being chiefly by exhalation of watery vapor from the skin.[2] In these instances the loss of water by transpiration is supplied constantly by the ingestion of large quantities of liquid.

Properties and Composition of the Sweat.—A very complete and satisfactory analysis of the sweat was made by Favre, in 1853. After taking every precaution to obtain the secretion in a perfectly pure state, he collected a very large quantity, nearly thirty pints (fourteen litres), the result of six transpirations from one person, which he assumed to represent about the average in composition.[3] The liquid was

[1] MACLAREN, *Training, in Theory and Practice*, London, 1866, p. 89.

[2] SOUTHWOOD SMITH, *The Philosophy of Health*, London, 1865, p. 284, *et seq.* Dr. Smith found great differences in the loss on different days in the same persons, and a great variation in the different persons employed in his experiments. In his third series of experiments, made upon ten workmen, the minimum of loss in one hour was two pounds. The maximum was in two persons "who worked in a very hot place for one hour and ten minutes." One of these lost four pounds and fourteen ounces, and the other, five pounds and two ounces.

[3] FAVRE, *Recherches sur la composition chimique de la sueur chez l'homme.*—*Archives générales de médecine*, Paris, 1853, 5me série, tome ii., p. 1, *et seq.*

The analysis of the sweat by Favre is the one most frequently referred to by

perfectly limpid, colorless, and of a feeble but characteristic odor. Almost all observers have found the reaction of the sweat to be acid; but it readily becomes alkaline on being subjected to evaporation, showing that it contains some of the volatile acids. In the experiments of Favre it was found that the fluid collected during the first half hour of the observation was acid, during the second half hour it was neutral or feebly alkaline, and during the third half hour, constantly alkaline. The specific gravity of the sweat is from 1003 to 1004.[1] The following is the composition of the fluid collected by Favre:

Composition of the Sweat.

Water		995·573
Urea		0·043
Fatty matters		0·014
Alkaline lactates		0·317
Alkaline sudorates		1·562
Chloride of sodium,	soluble in water	2·230
Chloride of potassium,	soluble in water	0·244
Alkaline sulphates,	soluble in water	0·012
Alkaline phosphates,	soluble in water	a trace.
Alkaline albuminates,	soluble in water	0·005
Alkaline earthy phosphates (soluble in acidulated water)		a trace.
Epidermic *débris* (insoluble)		a trace.
		1,000·000

We have already alluded to the functions of the skin as a respiratory organ and its office in regulating the temperature of the body by evaporation of what is known as the insensible perspiration; but the composition of the sweat indicates clearly that the skin is an important organ of excretion. Urea is now known to be a constant constituent of

physiological writers. The subject of the experiment, the surface being first thoroughly cleansed, was enclosed in a metallic case, exposed to an elevated temperature, and the transpiration collected as it flowed, and almost immediately analyzed. Each experiment was continued for from an hour to an hour and a half.

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 621.

the sweat,[1] and the compounds of sudoric acid are probably excrementitious in their character, although they have not yet been detected in the blood or in any of the tissues. The quantity of urea, under ordinary conditions, is not large; but it is well known that its proportion in the sweat is very much increased when there is deficient elimination by the kidneys. The sudoric acid, obtained by decomposition of the sudorates of soda and of potassa, is a nitrogenized substance, with a formula, according to Favre,[2] who first described it, of $C_{10}H_8O_{13}N$. The nature of the volatile acid has not yet been determined. The fatty matters are probably produced by the sebaceous glands, and the ordinary nitrogenized matters are derived from the epidermic scales. With regard to the inorganic constituents, there is no great interest attached to any but the chloride of sodium, which exists in a proportion many times greater than that of all the other inorganic matters combined.

Peculiarities of the Sweat in Certain Parts.—In the axilla, the inguino-scrotal region in the male, and the inguino-vulvar region in the female, and between the toes, the sweat always has a peculiar odor, more or less marked, which, in some persons, is excessively disagreeable. Donné

[1] Fourcroy, according to Berzelius, first indicated the presence of urea in the sweat of the horse; and afterward Landerer, Schottin (in cases of renal disease), Favre, Funcke, and others detected it in the sweat of the human subject. Funcke obtained it in a much larger proportion than is given by Favre. The presence of uric acid has never been determined.

—— FOURCROY, quoted by BERZELIUS, *Traité de chimie*, Paris, 1833, tome vii. Berzelius does not give any distinct reference to this observation, and it is not to be found in the earlier works of Fourcroy.

—— LANDERER, *Découverte de l'urée dans la transpiration.—Journal de chimie médicale*, Paris, 1848, série iii., tome iv., p. 475.

—— SCHOTTIN, *Ueber die chemischen Bestandtheile des Schweisses.—Archiv für physiologische Heilkunde*, Stuttgart, 1852, Bd. xi., S. 87.

—— FUNCKE, *Bieträge zur Kenntniss der Schweisssecretion.*—MOLESCHOTT'S *Untersuchengen*, Frankfurt a. M., 1858, Bd. iv., S. 56. In one observation Funcke found 0·112, and in another, 0·199 per cent. of urea in the sweat.

[2] FAVRE, *loc. cit.*

has shown that whenever the secretion has an odor of this kind its reaction is distinctly alkaline; and he is disposed to regard its peculiar characters as due to a mixture of the secretion of the other follicles found in these situations.[1] Sometimes the sweat about the nose has an alkaline reaction. In the axillary region, the secretion is rather less fluid than on the general surface and frequently has a yellowish color, so marked, sometimes, as to stain the clothing. The odor is probably due to the presence of volatile, odorous compounds of the fatty acids, like the caproates, the valerates, or the butyrates; but the presence of these principles has never been accurately determined.

[1] Donné, *Cours de microscopie*, Paris, 1844, p. 207.

CHAPTER V.

PHYSIOLOGICAL ANATOMY OF THE KIDNEYS.

Situation, form, and size of the kidneys—Coats of the kidneys—Division of the substance of the kidneys—Pelvis, calices, and infundibula—Pyramids—Cortex—Columns of Bertin—Pyramidal substance—Pyramids of Ferrein—Tubes of Bellini—Cortical substance—Malpighian bodies—Convoluted tubes—Narrow tubes of Henle—Intermediate tubes—Distribution of blood-vessels in the kidney—Vessels of the Malpighian bodies—Plexus around the convoluted tubes—Veins of the kidney—Stars of Verheyn—Lymphatics and nerves of the kidney—Summary of the physiological anatomy of the kidney.

THE urine is generally regarded by physiologists as the type of the excrementitious fluids, it having no function to perform in the economy, but being simply retained in the bladder to be voided at convenient intervals. All the re marks, indeed, that have been made concerning excretion in general may be applied without reserve to the action of the kidneys; and there are few subjects in physiology of greater interest than the process of urinary excretion, with its relations to nutrition and disassimilation. In entering upon the study of the functions of the kidneys, it will be found useful to consider certain points in their anatomy.

The kidneys are symmetrical organs, situated beneath the peritoneum in the lumbar region, invested by a proper fibrous coat, and always surrounded by more or less adipose tissue. They usually extend from the eleventh or twelfth rib downward to near the crest of the ilium; and the right is always a little lower than the left. In shape, the kidney is very

aptly compared to a bean; and the concavity, the deep, central portion of which is called the hilum, looks inward toward the spinal column. The weight of each kidney is from four to six ounces, usually about half an ounce less in the female than in the male. The left kidney is nearly always a little heavier than the right.

Outside of the proper coat of the kidney is a certain amount of fatty tissue enclosed in a loose fibrous structure. This is sometimes called the adipose capsule; but the proper coat consists of a close net-work of the ordinary white fibrous tissue, interlaced with numerous small fibres of the elastic variety. This coat is thin, smooth, and readily removed from the surface of the organ. At the hilum it is continued inward to line the pelvis of the kidney, covering the calices and blood-vessels. This coat, however, is not continued into the substance of the kidney.

On making a longitudinal section of the kidney, it presents a cavity at the hilum, bounded internally by the dilated origin of the ureter. This is called the pelvis. It is lined by a smooth membrane, which is simply a continuation of the proper coat of the kidney, and which forms little cylinders, called calices, into which the apices of the pyramids are received. Some of the calices receive the apex of a single pyramid, while others are larger, and receive two or three. The calices unite into three short, funnel-shaped tubes, called infundibula, corresponding respectively to the superior, middle, and inferior portions of the kidney. These finally open into the common cavity, or pelvis. The substance of the kidney is composed of two distinctly-marked portions called the cortical, and the medullary, or pyramidal.

The cortical substance is reddish and granular, rather softer than the pyramidal substance, and is about one-sixth of an inch in thickness. This occupies the exterior of the kidney, and sends little prolongations (columns of Bertin[1])

[1] BERTIN, *Mémoire pour servir à l'histoire des reins.—Mémoires de l'Académie Royale des Sciences, année*, 1744, Paris, 1748, p. 77.

between the pyramids. The surface of the kidney is marked by little polygonal divisions, giving it a lobulated appearance. This, however, is simply due to the arrangement of the superficial blood-vessels. The medullary substance is arranged in the form of pyramids, sometimes called the pyramids of Malpighi, from twelve to fifteen or eighteen in number, their bases presenting toward the cortical substance, and their apices being received into the calices at the pelvis. Ferrein subdivided the pyramids of Malpighi into smaller pyramids (the pyramids of Ferrein), each formed by about one hundred tubes radiating from the openings at the summit of the pyramids toward their bases.[1] The tubes composing these pyramids were supposed to pass into the cortical substance, forming corresponding pyramids of convoluted tubes, thus dividing this portion of the kidney into lobules, more or less distinct. The medullary substance is firm, of a darker red color than the cortical substance, and is marked by tolerably distinct striæ, which take a nearly straight course from the bases to the apices of the pyramids. As these striæ indicate the direction of the little tubes that constitute the greatest part of the medullary substance, this is sometimes called the tubular portion of the kidney.

There are few subjects connected with the physiological anatomy of the organism that present greater interest than the minute anatomy of the kidney; and this is one of the organs which has been most closely and persistently studied by anatomists. Without referring in detail to the investigations of Malpighi,[2] whose name is attached to the corpuscles of the cortical substance, Bellini,[3] who first studied the straight tubes, Ferrein,[4] who described the tubes of the corti-

[1] FERREIN, *Sur la structure des viscères nommés glanduleux, et particulièrement sur celle des reins et du foie.—Mémoires de l'Académie Royale des Sciences, année,* 1749, Paris, 1753, p. 499, *et seq.*

[2] MALPIGHIUS, *Opera Omnia*, Lond., 1686, tomus secundus, *De Renibus.*

[3] BELLINI, *Exercitationes Anatomicæ duæ de Structura et Usu Renum ut et de Gustus Organo*, Lugd. Batav., 1711.

[4] *Op. cit.*

cal substance, and other of the earlier anatomists, we shall proceed to study the structure of the kidney as it appears at the present day from the researches of later anatomists, who have brought to bear upon their investigations more perfect methods of injection and the improved microscopes now in use. Among the authors whose researches have developed the views now held by the best anatomists, may be mentioned Henle,[1] Bowman,[2] Goodsir,[3] Müller,[4] Gerlach,[5] Kölliker,[6] Toynbee,[7] Huschke,[8] Isaacs,[9] with some quite recent German and French observers, who have lately advanced new and interesting views that have an important bearing upon the mechanism of the secretion of urine.

The arrangement of the secreting portion of the kidneys classes them among the tubular glands, presenting a system of tubes, or canals, some of which are supposed simply to carry off the urine, while others separate the excrementitious constituents of this fluid from the blood. It is difficult to determine precisely where the secreting tubes merge into the excretory ducts, but it is the common idea that the cortical substance is the active portion, while the tubes of the pyramidal portion simply conduct away the excretion.[10]

[1] HENLE, *Traité d'anatomie générale*, Paris, 1843, tome ii., p. 503, *et seq.*, and *Zur Anatomie der Niere*, Gottingen, 1862.

[2] BOWMAN, *On the Structure and Use of the Malpighian Bodies of the Kidney.—Philosophical Transactions*, London, 1842, p. 57, *et seq.*

[3] GOODSIR, *London and Edinburgh Monthly Journal of Medical Science*, London and Edinburgh, 1842, p. 474.

[4] MUELLER, *Manuel de physiologie*, Paris, 1851, tome i., p. 369, *et seq.*

[5] GERLACH, *Beiträge zur Structurlehre der Niere.*—MÜLLER'S *Archiv*, 1845, S. 378, in CANSTATT'S *Jahresbericht*, Erlangen, 1846, S. 36.

[6] KÖLLIKER, *Ueber Flimmerbewegung in den Primordialnieren*, Idem, S. 36.

[7] TOYNBEE, *On the Minute Structure of the Human Kidney.—Medico-Chirurgical Transactions*, London, 1846, vol. xxix., p. 303, *et seq.*

[8] HUSCHKE, *Encyclopédie anatomique, Splanchnologie*, Paris, 1845, tome v., p. 285, *et seq.*

[9] ISAACS, *Researches into the Structure and Physiology of the Kidney*, and *On the Function of the Malpighian Bodies of the Kidney.—Transactions of the New York Academy of Medicine*, New York, 1857, vol. i., p. 377, *et seq.*

[10] TODD AND BOWMAN, *Physiological Anatomy and Physiology of Man*, Phila-

Pyramidal Substance.—Each papilla, as it projects into the pelvis of the kidney, presents from ten to twenty-five little openings, measuring from $\frac{1}{300}$ to $\frac{1}{60}$ of an inch in diameter.[1] The tubes leading from the pelvis immediately divide at very acute angles, generally dichotomatously, until a bundle of tubes arises, as it were, from each opening. These bundles constitute the pyramids of Ferrein. In their course, the tubes are slightly wavy and nearly parallel with each other. These are called the straight tubes of the kidney, or the tubes of Bellini. They extend from the apices of the pyramids to their bases, and pass then into the cortical substance. The pyramids contain, in addition to the straight tubes, a delicate fibrous matrix and numerous blood-vessels; which latter, for the most part, pass beyond the pyramids, to be finally distributed in the cortical substance. Recent researches have shown that some of the convoluted tubes dip down into the pyramids, returning to the cortical substance in the form of loops. This arrangement will be fully described in connection with the cortical portion.

The tubes of the pyramidal substance are composed of a strong, structureless basement-membrane, lined with granular, nucleated cells. According to the researches of Bowman, the tubes measure from $\frac{1}{500}$ to $\frac{1}{200}$ of an inch in diameter at the apices, and near the bases of the pyramids their diameter is about $\frac{1}{500}$ of an inch.[2] The membrane of the tubes is dense and resisting, and portions of it with the epithelial lining removed can generally be seen in microscopical examinations, when the pyramidal substance has been simply lacerated with needles. This membrane is from $\frac{1}{50000}$ to $\frac{1}{20000}$ of an inch in thickness.[3]

The cells lining the straight tubes exist in a single layer

delphia, 1857, p. 789. This is the idea advanced in nearly all works on physiology, when any opinion is expressed with regard to the relative activity of the cortical and the pyramidal portions of the kidney.

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 488.

[2] TODD AND BOWMAN, *op. cit.*, p. 793.

[3] KÖLLIKER, *Microscopic Anatomy*, London, 1860, p. 406.

applied to the basement-membrane. They are thick, irregularly-polygonal in shape, and contain numerous albuminoid granules. They present one, and occasionally, though rarely, two granular nuclei with one or two nucleoli. They are very liable to alteration, and are only seen in the normal condition in a perfectly fresh, healthy kidney. Their diameter is about $\frac{1}{1500}$ of an inch. The caliber of the tubes is reduced by the thickness of their lining epithelium to $\frac{1}{900}$ or $\frac{1}{800}$ of an inch.

Cortical Substance.—In the cortical portion of the kidney are found numerous tubes, differing somewhat from the tubes of the pyramidal portion in size and in the character of their epithelial lining, but presenting the most marked difference in their direction. These tubes are somewhat larger than the tubes of pyramidal substance, and are very much convoluted, interlacing with each other inextricably in every direction. Scattered pretty uniformly through this portion of the kidney, are rounded or ovoid bodies, about four times the diameter of the convoluted tubes, known as the Malpighian bodies. At one time there was considerable difference of opinion with regard to the relation of these bodies to the tubes; but the researches of Bowman, Isaacs, and later anatomists, have established, without doubt, the fact that they are simply flask-like terminal dilatations of the tubes themselves.

As the result of the researches of Bowman, Goodsir, and Isaacs, the cortical portion of the kidney is now regarded as presenting a delicate fibrous matrix,[1] which forms a sort of skeleton for the support of the secreting portion with its blood-vessels. The tubes of this portion are convoluted and somewhat larger than the straight tubes, but are continuous with them, terminating finally in the Malpighian bodies.

[1] The fibrous matrix of the kidney was first described in detail by Goodsir, in 1842 (*loc. cit.*), but its existence was afterward denied by such eminent anatomists as Henle, Frerichs, and others. This structure was very accurately described by Isaacs (*op. cit.*), and has since been admitted by most observers.

The researches of late anatomists, however, particularly in Germany, have shown that this simple view of the course and termination of the tubes of the cortical substance must be somewhat modified; though as far as the anatomy of the organ has any bearing upon our ideas concerning the mechanism of the secretion of urine, the views of physiologists need undergo no material change. However interesting the subject might be, it would be out of place to follow out critically and in detail all the recent investigations into the anatomy of these parts, and we shall simply describe the structure, direction, and relations of the tubes of the cortical substance, as they appear from the most reliable modern investigations.

The tubes of the cortical substance present considerable variations in size, and instead of a single system continuous with the straight tubes and terminating in the Malpighian bodies, we can distinguish three well-defined varieties:

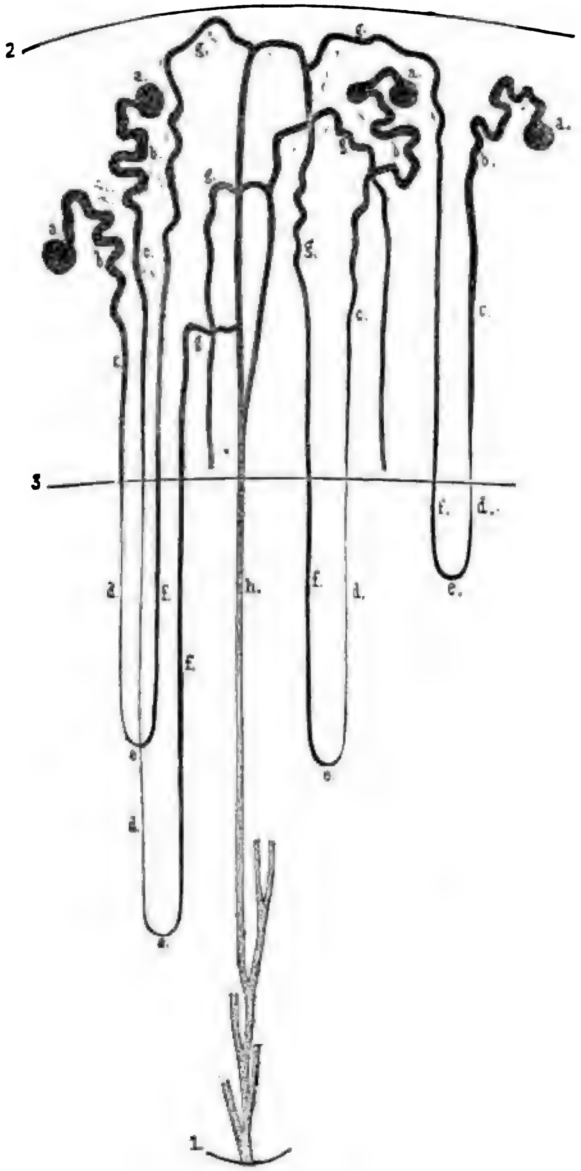
1. The ordinary convoluted tubes, directly connected with the Malpighian bodies. 2. Small tubes, continuous with the convoluted tubes, dipping down into the pyramids and returning to the cortical portion in the form of loops. 3. Large, communicating tubes, forming a plexus connecting the different varieties of tubes with each other and finally with the straight tubes of the pyramidal portion.

The relation of these tubes can be better understood by reference to Fig. 7, taken from a recent work by Dr. Ch. F. Gross.[1] This represents diagrammatically the course of a uriniferous canal in the human subject. 1, Surface of a renal papilla; 2, surface of the kidney; 3, boundary of the pyramidal substance; *a*, *a*, Malpighian corpuscles; *b*, *b*, convoluted tubes; *c*, *c*, straight portion of the tubes; *d*, *d*, narrow tubes of Henle; *e*, *e*, loops; *f*, *f*, large tubes of Henle; *g*, *g*, communicating tubes, uniting with several others to form *h*, a tube of Bellini.

In tracing out the course and the relations of the tubes,

[1] Gross, *Essai sur la structure microscopique du rein*, Strasbourg, 1868.

Fig. 7.



which recent observations have shown to be somewhat intricate, it will be found most convenient to commence with a description of the Malpighian bodies, and follow the course of the tubes from these bodies to their connections with the straight tubes of the pyramidal substance.

Malpighian Bodies.—These are ovoid or rounded terminal dilatations of the convoluted tubes, of somewhat variable size, measuring from $\frac{1}{250}$ to $\frac{1}{100}$ of an inch in diameter. They are composed of a membrane continuous with that which forms the convoluted tubes, of the same homogeneous character, but somewhat thicker, measuring about $\frac{1}{20000}$ of an inch, while the membrane of the tubes is only about $\frac{1}{40000}$ of an inch in thickness. This sac—sometimes called the capsule of Müller—encloses a mass of convoluted blood-vessels, and is lined with a layer of nucleated epithelial cells. The question of the existence of epithelium within the Malpighian body and the anatomical characters of the cells have been the subject of considerable discussion. Bowman, in his original essay on the kidney, makes the statement repeatedly that the vessels are bare within the capsule; and this has led some authors to suppose that he did not recognize the presence here of any epithelium whatsoever. This view favors the idea that the Malpighian bodies separate only water from the blood, and that the cells lining the convoluted tubes secrete the solid principles of the urine. Bowman has never denied the existence of epithelium within the capsule, but he regards it as of a different character from that lining the tubes. His statement with regard to it is as follows: "The epithelium is continued in many cases over the whole inner surface of the capsule; in other instances I have found it impossible to detect the slightest appearance of it over more than a third of the capsule."[1] There can be no doubt with regard to the constant presence of epithelial cells within the capsule of the Malpighian bodies, particularly since the researches of Gerlach, by whom they were

[1] Bowman, *op. cit.*, p. 60.

accurately described and figured, in 1845,[1] and the later confirmatory observations of Kölliker,[2] Isaacs,[3] and numerous other anatomists. It only remains to describe the characters of the cells as compared with those lining the convoluted tubes, and to ascertain whether they line the capsule alone, or are also attached to the vascular tuft.

Bowman believed that the cells, when they existed, simply lined the capsule, and that the blood-vessels were entirely bare; while Gerlach described cells attached to the blood-vessels, and Isaacs regarded these cells as entirely different from those attached to the membrane. From the great number of observations made by Isaacs upon the kidneys of different animals, there can be hardly any doubt concerning the correctness of the latter view; for not only did he describe minutely the difference between the cells of the capsule and those attached to the tuft, but he found that the walls of the cells of the capsule were dissolved by dilute nitric acid, "while comparatively little effect was produced upon those of the tuft, thus showing a difference in their constitution and organization."[4] We must, therefore, recognize in the Malpighian body two varieties of cells, differing in size, form, and situation; one variety lining the capsule, and the other covering the vascular tufts.

Nearly all observers who have studied the anatomy of the kidney practically agree that the cells attached to the capsule are smaller and more transparent than those lining the convoluted tubes. They are ovoid, nucleated, and finely granular. The cells covering the vessels, however, are larger and more opaque, and resemble the epithelium lining the tubes. They measure from $\frac{1}{1400}$ to $\frac{1}{1000}$ of an inch in diameter, by about $\frac{1}{2500}$ of an inch in thickness.

Tubes of the Cortical Substance.—Following out the tubes in the cortical substance from the Malpighian bodies, we find first a short, constricted portion, which has sometimes

[1] GERLACH, *op. cit.* [2] *Loc. cit.* [3] *Loc. cit.* [4] ISAACS, *op. cit.*, p. 405.

been called the neck of the capsule. The tube soon dilates to the diameter of about $\frac{1}{500}$ of an inch, when its course becomes exceedingly intricate and convoluted. These are what have been known as the convoluted tubes of the kidney. The membrane of these tubes is transparent and homogeneous, but quite firm and resisting. It measures about $\frac{1}{40000}$ of an inch in thickness. It is lined throughout with a single layer of rounded or irregularly-polygonal epithelial cells, from $\frac{1}{1400}$ to $\frac{1}{1000}$ of an inch in diameter, somewhat larger, consequently, than the cells lining the straight tubes. These cells are nucleated and usually quite granular. It has been found that in many of the lower orders of animals, the cells lining the neck of the capsule are provided with vibratile cilia. Bowman has described ciliated epithelium in the kidneys of reptiles,[1] and Johnson speaks of the cilia as found in other classes.[2] Isaacs has observed feeble movements in cells from the kidneys of some of the mammalia,[3] and it is possible that they may exist in man, though their presence has never been actually demonstrated.

The course of the tubes, after they have lost the characters which were formerly supposed to be peculiar to the tubes of the cortical substance, and their anastomoses, have attracted much attention within the last few years. It has been shown by Henle, and the most important points in his observations have been confirmed by numerous anatomists, that the convoluted tubes, instead of connecting directly with the tubes of the pyramidal substance, are continuous with a system of smaller tubes, which pass into the pyramids in the form of loops.[4]

Narrow Tubes of Henle.—According to the most recent observations, the convoluted tubes above described,

[1] *Op. cit.*, p. 73.

[2] JOHNSON, *Cyclopædia of Anatomy and Physiology*, London, 1847–1849, vol. iv., part i., p. 246, Article, *Ren.*

[3] *Op. cit.*, p. 383.

[4] Henle first described looped tubes of very small diameter projecting into the pyramidal substance, but did not fully recognize the connections of these

after a long and tortuous ramification in the cortical substance, invariably become continuous, near the pyramids, with tubes of much smaller diameter, which form loops, extending to a greater or less depth into the pyramids. The loops formed by these canals (the narrow tubes of Henle) are nearly parallel with the tubes of Bellini, and are much more numerous near the bases of the pyramids than toward the apices.[1] The diameter of these tubes is very variable, and they present enlargements at irregular intervals in their course. The narrow portions are about $\frac{1}{2000}$ of an inch in diameter, and the wide portions, about twice this size. According to Gross, this narrow portion is never absent, and is lined by small, clear cells with very prominent nuclei.[2] The wider portions are lined by larger granular cells. Near the bases of the pyramids, the wide portion sometimes forms the loop; but near the apices, the loop is always narrow. The difference in the size of the epithelium is such, that while the diameter of the tube is variable, its caliber remains nearly uniform. The membrane of these tubes is quite thick, thicker, even, than the membrane of the tubes of Bellini.

Intermediate Tubes.—After the narrow tubes of Henle have returned to the cortical substance, they communicate with a system of flattened, ribbon-shaped canals, measuring from $\frac{1}{1200}$ to $\frac{1}{1000}$ of an inch in diameter, with excessively thin, fragile walls, lined by clear pavement-epithelium. These tubes take an irregular and somewhat angular course between the true convoluted tubes, and finally empty into the branches of the straight tubes of Bellini, thus estab-

tubes with the large convoluted tubes of the cortical substance and the tubes of Bellini, as has been done by later investigators. An excellent review of the views of Henle on this subject is given by Gross (*loc. cit.*, p. 6, *et seq.*). The connection of these tubes with the ordinary convoluted tubes, and through them with the Malpighian bodies, has been fully established by the very elaborate researches of Schweigger-Seidel. (*Die Nieren des Menschen*, Halle, 1865, Taf. iv.)

[1] Most of the facts with regard to these looped canals we have recently been enabled to verify in a very elegant section of the kidney of the human subject, prepared by Dr. R. T. Edes, of Boston Highlands, Mass.

[2] Gross, *op. cit.*, p. 26.

lishing a communication between the tubes coming from the Malpighian bodies and the tubes of the pyramidal substance. They are called the intermediate tubes, or the canals of communication. Some observers have described them as forming an anastomosing plexus, but this disposition is not definitely established.

The tubes into which the intermediate canals open join with others, generally two by two, and pass in a nearly straight direction into the pyramids, where they continue to unite with each other in their course, becoming, consequently, less and less numerous, until they open at the apices of the pyramids into the infundibula and the pelvis of the kidney.

Distribution of Blood-vessels in the Kidney.—The blood-vessels of the kidney present certain interesting peculiarities in their distribution, which have been very successfully studied by Bowman, Isaacs, and many other anatomists, by means of minute injections of the renal arteries and veins. With the improved methods of injection now employed, their arrangement can be readily followed.

The renal artery, which is quite voluminous in proportion to the size of the kidney, enters at the hilum, and divides into four branches. By numerous smaller branches it then penetrates between the pyramids, and ramifies in the columns of cortical substance which occupy the spaces between the pyramids (columns of Bertin). The main vessels, which are generally two in number, occupy the centre of the columns of Bertin, sending off in their course, at short intervals, regular branches on either side toward the pyramids. When these branches reach the boundary of the cortical substance, they turn upward and follow the periphery of the pyramid to its base. Here the vessels form an arched, anastomosing plexus, which is situated exactly at the boundary which separates the rounded base of the pyramid from the cortical substance. This plexus presents a convexity looking toward the cortical substance, and a concavity toward the pyra-

mid. It is so arranged that the interstices are just large enough to admit the collections of tubes that form the so-called pyramids of Ferrein.

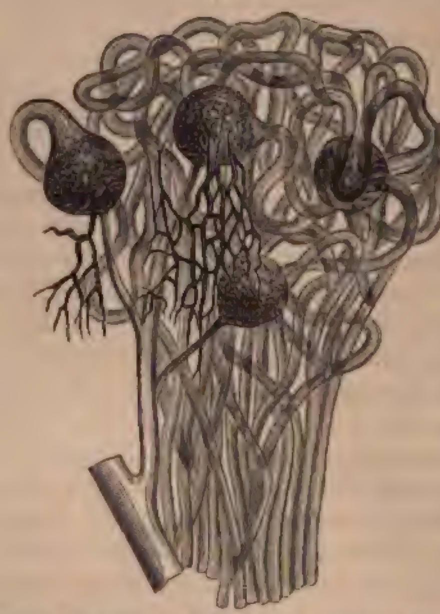
From this arcade of vessels, branches are given off in two opposite directions. From its concavity, numerous small branches, measuring at first from $\frac{1}{1200}$ to $\frac{1}{750}$ of an inch in diameter, pass downward toward the papillæ, giving off small ramifications at very acute angles, and becoming reduced in size to about $\frac{1}{2500}$ of an inch. These vessels—called sometimes the arteriolæ rectæ—surround the straight tubes and pass into capillaries in the substance of the pyramids and at their apices.

From the convex surface of the arterial arcade, numerous branches are given off at nearly right angles. These pass into the cortical substance, breaking up into a large number of little arterial twigs, from $\frac{1}{1500}$ to $\frac{1}{500}$ of an inch in diameter, which penetrate the Malpighian bodies at a point opposite to the origin of the convoluted tubes. Once within the capsule, the arteriole breaks up into from five to eight branches, which then divide dichotomatously into vessels measuring from $\frac{1}{3000}$ to $\frac{1}{1500}$ of an inch in diameter, arranged in the form of coils and loops, constituting a dense, rounded mass (the Malpighian coil), filling up the capsule. These vessels break up into capillaries without anastomoses. Their coats are amorphous and provided with numerous nuclei rather shorter than those found in the general capillary system.

The blood is collected from the vessels of the Malpighian bodies by veins, sometimes one, and frequently three or four, which pass out of the capsule and form a second capillary plexus surrounding the convoluted tubes. When there is but one vein, it emerges near the point of penetration of the arteriole. The walls of the vein are much more fragile than those of the arteriole, and consequently, in ordinary microscopical preparations of the cortical substance, the arteriole is left attached, while the veins are torn off.

The efferent vessels, immediately after their emergence from the capsule, break up into a very fine and delicate plexus of capillaries, closely surrounding the convoluted tubes. These form a true plexus, the branches anastomosing freely in every direction; and the distribution of vessels in this part resembles essentially the vascular arrangement in the glands generally. Bowman has called the branches which connect together the vessels of the Malpighian tuft and the capillary plexus surrounding the tubes, the portal system of the kidney.[1] These intermediate vessels form a coarse plexus around the prolongations of the pyramids of Ferrein into the cortical substance.

Fig. 8.



Malpighian bodies, injected, and convoluted tubes from the kidney of the sheep. (Isaacs, *Structure and Physiology of the Kidney.—Transactions of the New York Academy of Medicine*, 1857, vol. i., p. 391.)

The renal or emulgent vein takes its origin, in part from the capillary plexus surrounding the convoluted tubes, and in part from the vessels distributed in the pyramidal substance. A few branches come from vessels in the envelopes of the kidney, but these are comparatively unimportant. The plexus surrounding the convoluted tubes empties into venous radicles, which pass to the surface of the kidney, and these present a number of little radiating groups, each converging toward a cen-

[1] Bowman, *op. cit.*, p. 63.

tral vessel. This arrangement gives to the vessels of the fibrous envelope of the kidney a peculiar stellate appearance. These are sometimes called the stars of Verheyn.[1] The large trunks which form the centres of these stars then pass through the cortical substance to the rounded bases of the pyramids, where they form a vaulted venous plexus corresponding to the arterial plexus already described. The vessels distributed upon the straight tubes of the pyramidal substance form a loose plexus around these tubes, except at the papillæ, where the net-work is much closer. They then pass into the plexus at the bases of the pyramids to join with the veins from the cortical substance. From this plexus a number of larger trunks arise and pass toward the hilum in the centre of the inter-pyramidal substance, enveloped in the same sheath with the arteries. Passing thus to the pelvis of the kidney, the veins converge into from three to four great branches, which unite to form the renal, or emulgent vein. A preparation of all the vessels of the kidneys shows that the veins are much more voluminous than the arteries.[2]

The lymphatics of the kidney are few, and, according to Sappey, only exist in the substance of the organ, converging toward the hilum. This author does not admit the existence of superficial lymphatics.

The nerves are quite numerous, and are derived from the solar plexus, their filaments following the artery in its distribution in the interior of the organ and ramifying upon the walls of the vessels.

[1] VERHEYN, *Anatomie*, Leipzig, 1714, S. 222.

[2] In a recent pamphlet on a circulation peculiar to the kidney of mammals, a French author assumes to have demonstrated an arrangement of blood-vessels in the cortical substance very different from that which we have described. The glandular character of the Malpighian bodies and their connection with the convoluted tubes are denied. There is apparently so little basis for these peculiar views, that it does not seem necessary to discuss them in detail. (SUCQUET, *D'une circulation du sang spéciale au rein des animaux vertébrés mammifères, et de la sécrétion des urines qu'elle y produit*, Paris, 1867.)

Summary of the Physiological Anatomy of the Kidney.—The division of the kidneys into the cortical and pyramidal substance is quite apparent to the naked eye. The pyramids are distinctly striated, and present, in this regard, and in their darker color, a marked difference from the cortical substance. At the apex of each pyramid there are from ten to twenty-five little orifices, from $\frac{1}{300}$ to $\frac{1}{80}$ of an inch in diameter, which connect with the straight tubes. From these openings the tubes branch at a very acute angle, each one leading to a bundle or system of straight canals, forming the collections called the pyramids of Ferrein. The branches of these tubes (the tubes of Bellini) are about $\frac{1}{500}$ of an inch in diameter, and are composed of a structureless membrane lined by nucleated epithelial cells.

When these tubes arrive at the bases of the pyramids and pass into the cortical substance, they increase slightly in size, and are lined with granular and rounded cells of epithelium. They then become excessively convoluted, connect with certain other tubes in their course, and after forming loop-like processes extending into the pyramids, finally terminate in rounded or ovoid dilatations (the Malpighian bodies). These dilated extremities measure from $\frac{1}{250}$ to $\frac{1}{100}$ of an inch in diameter.

The Malpighian bodies are composed of a fibrous capsule (the capsule of Müller), and each one contains a mass of convoluted blood-vessels surrounded by nucleated epithelial cells.

The loop-like processes dip down into the pyramids and return to the cortical substance, present a filamentous, constricted portion, and are here called the narrow tubes of Henle. The communicating tubes, which connect these canals with the straight tubes of the pyramidal substance, are sometimes called "intermediate tubes." They are flattened or ribbon-shaped, with very delicate walls, and are lined by transparent pavement-epithelium.

Throughout the kidney there is a delicate stroma of fibrous tissue, in the meshes of which are lodged the blood-

vessels, the straight tubes of the pyramidal substance, and the tubes and Malpighian bodies of the cortical substance.

The renal artery penetrates the kidney at the hilum, sends branches between the pyramids, which are distributed in the form of an arched arterial plexus over the upper portion and the bases of the pyramids, following exactly the boundary between the pyramidal and the cortical substance. From these vessels, branches are given off both on the convexity and the concavity of the arches. Numerous small branches (arteriolæ rectæ) pass downward along the straight tubes toward the papillæ, becoming capillary as they surround the tubes. Other branches take an opposite direction and pass into the cortical substance, breaking up into little twigs, each one of which penetrates a capsule of Müller and divides in its interior into a mass of looped, convoluted vessels which constitute the Malpighian coil. The blood is carried away from the Malpighian bodies by one, two, or three vessels, which are then immediately distributed in a close plexus around the tubes of the cortical substance. From this plexus, the radicles of the renal vein pass to the surface of the kidney, where they present a stellate arrangement, converging toward several large central vessels (the stars of Verheyn). These central vessels penetrate the cortical substance and form an arched venous plexus over the rounded bases of the pyramids. This plexus also receives by its concave surface venous branches from the pyramidal substance. The blood is then emptied into larger veins, passing between the pyramids in the same sheath with the arteries, to form the renal or emulgent vein.

CHAPTER VI.

MECHANISM OF THE FORMATION AND DISCHARGE OF URINE.

Formation of the excrementitious constituents of the urine in the tissues, absorption of these principles by the blood, and separation of them from the blood by the kidneys—Effects of removal of both kidneys from a living animal—Effects of tying the ureters in a living animal—Extirpation of one kidney—Influence of blood-pressure, the nervous system, etc., upon the secretion of urine—Effects of the destruction of all the nerves going to the kidneys—Alternation in the action of the kidneys upon the two sides—Changes in the composition of the blood in passing through the kidneys—Physiological anatomy of the urinary passages—Mechanism of the discharge of urine.

The striking peculiarities which the kidney presents in its structure, as compared with the true glands, and the fact of the voluntary discharge of its secretion at certain intervals, would naturally lead to a closer study of the mechanism of the production and discharge of the urine, than we have given under the general head of mechanism of the formation of the excretions. The composition of the urine, also, will be found to be exceedingly complex, and its various ingredients bear the closest relation to the processes of nutrition and disassimilation; all of which considerations render it of the greatest importance to ascertain the precise mode of its formation, and to study all the conditions by which this process may be modified. In the present state of our knowledge, we must certainly regard the excrementitious constituents of the urine as formed essentially in the system at large, and merely separated from the blood by the kidneys; and a consideration of these effete principles belongs to the

subject of nutrition. It remains for us, then, in this connection, to treat, in general terms, of the way in which these substances find their way into the urine.

The most important constituent of the urine is urea; a crystallizable nitrogenized substance, which is discharged by the skin as well as by the kidneys. This has long been recognized as an excrementitious principle; but the first observations that gave any definite idea of the mechanism of its production were made by Prévost and Dumas,[1] in 1821. At the time these experiments were made, chemists were not able to detect urea in the normal blood; but Prévost and Dumas extirpated the kidneys from living animals (dogs and cats), and found an abundance of urea in the blood, after certain symptoms of blood-poisoning had been manifested. The first experiments were performed by removing one kidney by an incision in the lumbar region, and at the end of three or four days, after the animal had recovered from the first operation, removing the other. After the second operation the animals lived for from five to nine days. For the first two or three days there were no symptoms of blood-poisoning. Watery discharges from the stomach and intestinal canal occurred after a few days, and finally stupor and other marked evidences of nervous disturbance supervened, when the presence of urea in the blood could be easily determined. These observations were confirmed and extended by Ségalas and Vauquelin, in 1822, who presented to the French Academy of Medicine a specimen of nitrate of urea extracted from the blood of a dog, taken sixty hours after extirpation of the kidneys, giving its proportion to the weight of blood employed.[2] A few years later, the observations of Prévost and Dumas were con-

[1] The observations of Prévost and Dumas, Ségalas, Marchand, and others, have already been referred to (see p. 25).

[2] SÉGALAS, *Sur des nouvelles expériences relatives aux propriétés médicamenteuses de l'urée, et sur le gendre de mort qui produit la noix vomique.*—*Journal de physiologie*, Paris, 1822, tome ii., p. 356.

firmed in the human subject. In this case urea was found to have accumulated in the blood as the consequence of an injury received in the lumbar region.[1]

Since that time, as the processes for the determination of urea in the animal fluids have been improved, this substance has been detected in minute quantity in the normal blood by Marchand,[2] Picard,[3] Poisseuille and Gobley,[4] and many others. Picard, indeed, carefully estimated and compared the proportions of urea in the renal artery and the renal vein, and found that the quantity in the blood was diminished about one-half in its passage through the kidneys.[5] According to Robin, who apparently accepts the results obtained by Picard, the blood in the renal vein contains much less urea, urates, creatine, creatinine, chloride of sodium, etc., than the blood of the renal artery.[6] Still later urea has been found by Wurtz to exist in the lymph and chyle in larger quantity even than in the blood.[7]

These facts, which have been almost universally regarded as established, have led physiologists to adopt the view that the peculiar excrementitious principles found in the urine are not produced by the kidneys, but are formed in the system by the general process of disassimilation, are taken up from the tissues by the blood, either directly or through the

[1] SHEARMAN, *Case of Mechanical Injury to the Kidneys, followed by Coma; Suppression of the Secretion of Urea by the Kidneys, and Absorption of the Urea into the Blood—Recovery.—The Monthly Journal of Medical Science*, Edinburgh and London, 1848, vol. viii. (New Series, vol. ii.), p. 666.

[2] MARCHAND, *Sur la présence de l'urée dans le sang.—Annales des sciences naturelles*, Paris, 1838, 2me série, tome x., p. 46.

[3] PICARD, *De la présence de l'urée dans le sang, Thèse*, Strasbourg, 1856.

[4] POISSEUILLE ET GOBLEY, *Recherches sur l'urée.—Comptes rendus*, Paris, 1859, tome xlix., p. 164, *et seq.* Poisseuille and Gobley found, as a rule, more urea in the arterial than in the venous system. The blood from the carotid contained 0·225 parts per 1000; that from the portal vein, 0·171; from the splenic vein, 0·225, from the renal veins, 0·164; and from the femoral vein, 0·186.

[5] *Op. cit.*, p. 38.

[6] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 117.

[7] See vol. ii., Lymph and Chyle, pp. 520, 528.

lymph, and are merely separated from the blood in the kidneys; and it has consequently been pretty generally assumed that nearly, if not all, the constituents of the urine preëxist in the circulating fluid. There is, indeed, no well-defined principle in the urine that has not been actually demonstrated in the blood. As an additional argument in favor of this view of the mechanism of the urinary excretion, it has been ascertained that when the kidneys are interrupted in their function, there is a tendency to the elimination of the excrementitious principles of the urine by the lungs, skin, and alimentary canal; and that these matters only accumulate in the blood after this vicarious effort has failed to effect their complete discharge.

These ideas have seemed to be so completely justified by facts, that they have been applied to the mechanism of excretion by other organs, such as the skin and the liver; but within a few years, the older observations with regard to nephrotomized animals have been discredited; and it has been asserted, as the result of experiment, that urea and the urates do not accumulate in the blood after removal of the kidneys, but that this result only follows when both ureters have been tied. The experiments on which this idea is based have been applied mainly to the pathology of uræmic intoxication, but it is evident that they bear directly upon the mechanism of excretion. It is not assumed, however, that excrementitious principles are not formed by the disassimilation of the tissues; but it is asserted that urea and the urates are produced in the kidneys by a transformation of the excrementitious matters, creatine, creatinine, etc., which exist in the blood. It is foreign to our purpose to discuss *in extenso* the pathological conditions produced by the retention of the urinary principles in the blood; and we shall consider this question only so far as it bears upon the physiology of excretion.

The original experiments of Prévost and Dumas are very strong arguments in favor of the view that has been so long

almost unquestioned; viz., that urea is simply separated from the blood by the kidneys; but the more recent observations of Bernard and Barreswil, Robin, and many others, while they confirm the first experiments on this subject, have added very considerably to our knowledge of the mechanism of uræmic poisoning after extirpation of the kidneys. The kidneys, it has been found, can readily be removed from living animals, dogs, cats, rabbits, etc., without any great disturbance immediately following the operation. Bernard and Barreswil found that animals from which both kidneys had been removed did not usually present any distinctive symptoms for a day or two after, except that they vomited and passed an unusual quantity of liquid from the intestinal canal. During this period, the blood never contained an abnormal quantity of urea; but the contents of the stomach and intestine were found to be highly ammoniacal. During this time, also, the secretions from the stomach and intestines, particularly the stomach, became continuous, as well as increased in quantity. Animals operated upon in this way usually live for four or five days, and then die in coma following upon convulsions. Toward the end of life, the secretion of gastric and intestinal fluids becomes arrested, probably from the irritating effects of ammoniacal decomposition of their contents, and then, and then only, urea is found to accumulate enormously in the blood.[1]

It is thought by Bernard that the hypersecretion by the gastric and intestinal mucous membrane, in nephrotomized animals, is an effort on the part of the system to eliminate the urea, which is decomposed by contact with these membranes into carbonate of ammonia. This view is sustained by the fact that when urea is introduced into the alimentary canal in living animals, it disappears almost immediately

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 36, *et seq.* These experiments were first published by Bernard and Barreswil in the *Archives générales de médecine*, Paris, 1847, tome xiii., p. 449.

and is replaced by the ammoniacal salts.[1] Consequently, after removal of the kidneys, we should not expect to find an increased quantity of urea in the blood, until its elimination by the mucous membrane of the alimentary canal has ceased; but the fact that it then accumulates in large quantity cannot be doubted.

The results obtained by other experimenters generally correspond with those of Bernard and Barreswill. It has also been ascertained, as was shown by Ségalas and Vauquelin, that urea is an active diuretic when injected in small quantity into the veins of a healthy animal;[2] and that in this case it does not produce any poisonous effects, but is immediately eliminated. But when urea is injected into the vascular system of a nephrotomized animal, it produces death in a very short time, with the characteristic symptoms of uræmic poisoning.[3] We have frequently removed both kidneys from dogs, and when the operation is carefully performed, the animals live for from three to five days. In some instances they have been known to live for twelve days or even longer, but death always takes place finally with symptoms of blood-poisoning.

The experiments which are supposed to show that urea and the urates are actually formed in the kidneys—to which we have already alluded—were made with the view of comparing the effects of removal of both kidneys with those produced by tying the ureters. According to the observations of Oppler, the blood contains much more urea after the ureters are tied than after removal of the kidneys.[4] Perls states, as the result of experiments on rabbits, that no accumulation of urea in the muscular substance can be proved

[1] BERNARD, *op. cit.*, p. 51.

[2] SÉGALAS, *loc. cit.*

[3] In these cases, the symptoms before death are precisely like those observed after simple removal of the kidneys, the only difference being, that they are produced more promptly.

[4] OPPLER, *Beiträge zur Lehre von der Urämie.*—VIRCHOW'S *Archiv*, Berlin, 1861, Bd. xxi., S. 260, *et seq.*

after removal of the kidneys; but that this occurs only after tying the ureters, and the quantity seems to be greatest in the first twenty-four or forty-eight hours after the operation.[1] Essentially the same results were obtained by Zalesky,[2] who asserts that the proportion of urea in the blood after removal of the kidneys in dogs is about the same as in the normal condition. These experiments, which are directly opposed in their results to the well-considered observations of Prévost and Dumas, Bernard and Barreswil, Ségalas, and many others, cannot be accepted, unless it be certain that all the necessary physiological conditions have been fulfilled. In the first place it was positively demonstrated, as early as 1847, that urea does not accumulate in the blood immediately after removal of the kidneys, but only toward the end of life, and then it is found in enormous quantity.[3] In the second place, it is well known that the operation of tying the ureters is followed by an immense pressure of urine in the kidneys, which not only disturbs the eliminative action of these organs, but affects most seriously the general functions.

[1] PERLS, in CANSTATT'S *Jahresbericht*, Würzburg, 1865, S. 194. The experiments of Perls are not sufficiently extended to be very satisfactory. Rejecting one experiment in which the animal was killed twenty-four hours after removal of the kidneys—when no accumulation of urea could be expected—there are three examinations of the muscular substance after death from removal of the kidneys, and four after death from tying the ureters. In an examination after removal of the kidneys, 2·32 parts per 1,000 of nitrate of urea were found; in the second, there were no crystals in the extract; and in the third there were slight traces of urea. These animals died three or four days after the operation. Five examinations were made of the muscular substance in animals that died after tying the ureters. In three of these examinations, urea was found in considerable quantity; and in the remaining two, urea was present in very small quantity in one instance, and in the other, it is not stated that any urea was found. No examinations were made of the blood. These experiments on the accumulation of urea in nephrotomized animals are hardly sufficient to overthrow the researches of Prévost and Dumas, and others by whom their observations have been confirmed.

[2] ZALESKY, *Untersuchungen über den uræmischen Process und die Function der Nieren*, Tübingen, 1865.

[3] BERNARD AND BARRESWIL, *loc. cit.*

Since the influence of the nervous system upon the secretions has been so closely studied, it is evident that the pain and disturbance consequent upon the accumulation of urine above the ligated ureters must have an important reflex action upon the secretions; and this would probably interfere with the vicarious elimination of urea and other excrementitious principles by the stomach and intestines. It is well known to practical physicians that an arrest of these secretions, in cases of organic disease of the kidneys, is liable to be followed immediately by evidences of uræmia, and that grave uræmic symptoms are frequently removed by the administration of remedies that act promptly and powerfully upon the intestinal canal. As additional evidence of the great disturbance of the system, aside from the mere accumulation of excrementitious principles in the blood, which must result from tying the ureters, we have the intense distress and general prostration, always so prominent in cases of nephritic colic, where there is only temporary obstruction of one ureter. The pathological condition of the kidneys which follows the operation of tying the ureters was observed by Richerand, many years ago,[1] and the observations of Oppler, Perls, and Zalesky, on this subject are not entirely novel.[2]

From a careful review of the important facts bearing upon this question, there does not seem to be any valid ground for a change in our ideas concerning the mode of elimination of urea and the other important excrementitious constituents of the urine. There is every reason to

[1] RICHERAND ET BÉRARD, *Nouveaux élémens de physiologie*, Paris, 1833, tome ii., p. 142.

Richerand noted great disturbance in animals, thirty-six hours after tying both ureters. In a cat on which this operation had been performed, death took place on the third day. "The kidneys were swollen, softened, and, as it were, macerated; all the organs, all the humors, and the blood itself, participated in this urinous diathesis." (*Loc. cit.*, p. 143.)

[2] MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1862, tome vii., pp. 457, 459.

suppose that these principles are produced in the various tissues and organs of the body during the process of disassimilation, are taken up by the blood, and are simply separated from the blood by the kidneys. There may be unimportant modifications of some of these principles in the kidneys or in the urine, such as the conversion of a certain amount of creatine into creatinine, but the great mass of excrementitious matter is separated from the blood by the kidneys unchanged.

Extirpation of one kidney from a living animal is not necessarily fatal. We have frequently performed this operation as a class-demonstration, and kept the animal for weeks and months, without observing any indications of disturbance in the eliminative functions. If the operation be carefully performed, the wound will generally heal without any difficulty, and in most instances the remaining kidney seems sufficient for the elimination of urine for an indefinite period. In all of our experiments, save one, the animals, killed long after the wound had healed, never presented any marked symptoms of the retention of excrementitious matters in the blood. It is a noticeable fact, however, that in many instances they showed a marked change in disposition, and the appetite became voracious and unnatural. These animals would sometimes eat fæces, the flesh of dogs, etc., and, in short, presented certain of the phenomena so frequently observed after extirpation of the spleen.

After extirpation of one kidney, it has been observed that the remaining kidney increases in weight, though recent investigations show that this is due mainly to an increase in the amount of blood, lymph, and urinary principles, and not to a new development of renal tissue. The earliest definite experiments upon this point are those of Valentin, who extirpated one kidney, on eight occasions, in rabbits, three of the observations being fully reported. In one animal, that lived twenty-two hours, the weights of the kidneys

were as 1 to 1·28; in another, that lived twenty-four hours, the weights were as 1 to 1·06; and in the third, that lived for eight days, the weights were as 1 to 1·45. This is taking the extirpated kidney as 1.[1] Rosenstein made a number of observations of the same kind on rabbits and dogs, with the following results: He first ascertained that the right kidney is normally heavier than the left: as 1 to 1·02; 1 to 1·05; 1 to 1·08; 1 to 1·12. After extirpation of one kidney, the remaining kidney became heavier, but without enlargement of the Malpighian bodies or convoluted tubes, and with very slight hypertrophy of the epithelium and interstitial tissue. He found, however, an excess of blood, lymph, and urinary matters.[2]

It is reasonable to suppose that Nature has provided, in the kidneys, more working substance than is absolutely required for the elimination of the excrementitious constituents of the urine; and that even when one kidney is removed, the other is competent to eliminate the amount of excrementitious matter that is produced, under ordinary conditions of the system.

The exceptional experiment in which the animal died after extirpation of one kidney is quite interesting: October 6, 1864, we removed one kidney from a small cur-dog, about nine months old, by an incision in the lumbar region. The animal did not appear to suffer from the operation, and the wound healed kindly. The only marked effects were great irritability of disposition and an exaggerated and perverted appetite. He would attack the other dogs in the laboratory without provocation, and would eat with avidity fæces, putrid dog's flesh, and articles which the other animals would not touch, and which he did not eat before the operation. On the morning of November 18th, forty-three

[1] VALENTIN, *De Functionibus Nervorum Cerebralium et Nervi Sympathetici*, Bernæ, 1839, p. 148.

[2] ROSENSTEIN, *Ueber complementäre Hypertrophie der Niere.—Archiv für pathologische Anatomie und Physiologie*, Berlin, 1871, Bd. lv., S. 143, *et seq.*

days after the operation, the dog appeared to be uneasy, cried frequently, and at 12 o'clock went into convulsions, which continued until 3½ P. M., when he died.

In one other instance, in which a dog was kept for more than a year after extirpation of one kidney, it was occasionally observed that the animal was rather quiet and indisposed to move for a day or two, but this always passed off, and when he was killed he was as well as before the operation.

Influence of the Nervous System, Blood-pressure, etc., upon the Secretion of Urine.—There are numerous instances in which very marked and sudden modifications in the action of the kidneys take place under the influence of fear, anxiety, hysteria, etc., when the impression must have been transmitted through the nervous system. Although little is known of the final distribution of the nerves in the kidney, it has been ascertained that here, as elsewhere, filaments from the sympathetic system ramify upon the walls of the blood-vessels, and thus are capable of modifying the quantity and the pressure of blood in these organs.

It may be stated as a general proposition, that an increase in the pressure of blood in the kidneys increases the flow of urine; and that when the blood-pressure is lowered, the flow of urine is correspondingly diminished. This fact will in a measure account for the increase in the flow of urine during digestion; but it cannot serve to explain all of the modifications that may take place in the action of the kidneys. The fact above stated, although it has been long recognized by physiologists, has lately been very fully illustrated by the experiments of Bernard. This observer measured the pressure of blood in the carotid artery of a dog, and carefully noted the quantity of urine discharged in the course of a minute from one of the ureters. Afterward, by tying the two crural, the two brachial, and the two carotid arteries, he increased the blood-pressure about one-half, and the quantity of urine discharged in a minute was immediately increased

by a little more than fifty per cent. In another animal, he diminished the pressure by taking blood from the jugular vein, and the quantity of urine was immediately reduced about one-half.[1] His later observations on this subject showed that the increase in the quantity of urine produced by exaggerated pressure of blood in the kidneys was capable of being modified through the nervous system. In these experiments, the nerves going to one kidney were divided, which produced an increase in the arterial pressure and a consequent exaggeration in the quantity of urine from the ureter on that side. The pressure was then farther increased by stopping the nostrils of the animal. The quantity of urine was increased by this on the side on which the nerves had been divided, but the pain and distress from want of air arrested the secretion upon the sound side.[2]

The precise influence which special nerves exert upon the secretion of urine has not yet been positively ascertained. Some important facts, however, bearing upon this subject have been developed of late years. In his interesting and novel experiments upon artificial diabetes in animals, Bernard found that when irritation was applied to the floor of the fourth ventricle, in the median line, exactly in the middle of the space comprised between the origin of the pneumogastrics and the auditory nerves, the urine was increased in quantity and became strongly saccharine. When the irritation was applied a little above this point, the urine was simply increased in quantity, but contained no sugar; and when the puncture was made a little below, sugar appeared in the urine, without any increase in the quantity of the secretion.[3] It has also been observed that section of the spinal cord in the upper part of the dorsal region arrests, for a time, the secretion of urine.[4]

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 155.

[2] Unpublished lectures delivered at the College of France in the Summer of 1861.

[3] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 339.

[4] BERNARD, Unpublished lectures, 1861.

Bernard, in following out his ideas with regard to the mechanism of secretion, supposes that there are certain nerves derived from the sympathetic system, the galvanization of which will arrest the flow of urine; and others, belonging to the cerebro-spinal system, called by him the motor nerves of the gland, which, when galvanized, should increase the flow of urine; but the kidney, unlike the true glandular organs, will continue to secrete for a time when removed from all nervous influence. He has divided the sympathetic nerves that penetrate with the blood-vessels at the hilum, and galvanized them, producing an arrest of secretion during the entire period of the galvanization.[1] With regard to the determination of the motor nerve of the kidney, the experiments are not so satisfactory; and while there may be nerves capable of exciting the secretion of urine, analogous to the motor nerves of the salivary glands, this has never been actually demonstrated.

The final effect of division of all the nerves going to the kidney is very curious. The immediate effect of destruction of these nerves is to increase largely the amount of blood sent to the kidney, the organ then pulsating like an aneurismal tumor. In experiments on this subject by Müller and Peipers, the flow of urine was sometimes arrested by division of these nerves, but occasionally it continued. In these observations, the nerves were destroyed by applying a ligature tightly to the vessels as they enter at the hilum, including every thing but the ureter. The ligature was then loosened, so as to admit the blood, but the nerves were bruised and destroyed.[2] We have just referred to the observations of Bernard, in which the flow of urine was temporarily increased by this operation. The secretion of urine continues, however, for only a few hours. It then ceases, and the nutrition of the kidney becomes profoundly affected, its tissue breaking down into a putrid, semi-

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 163.

[2] MUELLER, *Manuel de physiologie*, Paris, 1851, tome i., p. 391.

fluid mass, which probably enters the blood and is the cause of death.

The other physiological conditions that affect the urinary excretion influence the composition of the urine and the quantity of excrementitious matters separated by the kidneys. These will be more appropriately considered under the head of nutrition and disassimilation. It is sufficient to remark, in this connection, that during digestion, when the composition of the blood is modified by the absorption of nutritive matters, the quantity of urine is usually increased. This is particularly marked when a large amount of liquid is taken. There are certain modifications due to the condition of the blood in disease, but these do not belong to the subject of physiology. The same may be said of the elimination of foreign matters introduced into the circulation, and the excretion of sugar by the kidneys when this substance is produced in the system in excess.

The prompt separation of certain matters from the blood by the kidneys has been illustrated by experiments upon animals, and by observations on the human subject in cases of extroversion of the bladder, in which the urine could be immediately collected as it flowed from the ureters. In a case of this kind observed by Erichsen, the ferrocyanide of potassium taken into the stomach after a fast of eleven hours appeared in the urine in one minute. In this case, numerous experiments were made with other articles, which it is unnecessary to follow out in detail.[1]

As the excrementitious principles eliminated by the kidneys are being constantly produced in the tissues by the process of disassimilation, the formation of urine is constant; presenting, in this regard, a marked contrast with the intermittent flow of most of the secretions proper, as distinguished

[1] ERICHSEN, *Observations and Experiments on the Rapidity of the Passage of some Foreign Substances through the Kidnies, and on some Points connected with the Excretion of the Urine.—London Medical Gazette*, London, June 27, 1845, New Series, vol. ii., p. 363.

from the excretions. It was noted by Erichsen,[1] in his case of extroversion of the bladder, and it has been farther shown by experiments upon dogs, that there is an alternation of action upon the two sides. Bernard exposed the ureters in a living animal and fixed a small silver tube in each, so that the secretion of both kidneys could be readily observed; and he noted that a large quantity of fluid was discharged from one side for from fifteen to thirty minutes, while the flow from the other side was slight and in some instances was entirely arrested. The flow then commenced with activity upon the other side, while the discharge from the opposite ureter was diminished or arrested.[2] We are already familiar with this mode of action in the parotid glands.[3]

Changes in the Composition of the Blood in passing through the Kidneys.—Some of the changes in the blood in its passage through the kidneys have already been noted. The most important of these consist in a diminution in the proportion of urea, the urates, and other of the excrementitious principles found in the urine. This would be expected, inasmuch as these principles are constantly present in the urine, and have been shown to be derived exclusively from the blood. It has been ascertained, also, that the blood of the renal veins contains less water than the blood of any other part of the venous system.[4] The constant separation of water from the blood by the kidneys, for the purpose of carrying off the soluble excrementitious principles, is an explanation of this fact. It was also observed by Simon, a number of years ago, that the blood of the renal veins does

[1] Erichsen, *loc. cit.*, p. 361. In this case, the openings of both ureters were exposed to view, and Erichsen states that "the two ureters do not open at the same time, but with an irregularly alternating action."

[2] Bernard, Unpublished lectures delivered at the College of France in the Summer of 1861. During the progress of this course of lectures, we had an opportunity of observing the alternate action of the two kidneys.

[3] See vol. ii., Digestion, p. 160.

[4] Robin, *Leçons sur les humeurs*, Paris, 1867, p. 80.

not coagulate readily, and that it is impossible to obtain fibrin from it in the ordinary way by stirring with rods.[1] It is difficult in the present state of our knowledge to give any satisfactory physiological explanation of this disappearance of fibrin in the kidneys. Absence of fibrin has also been noted by Lehmann in the blood of the hepatic veins.[2]

Reference has already been made to the researches of Bernard, showing that the blood coming from many of the glands during their functional activity is but little darker than arterial blood.[3] The action of the kidneys is constant, and the quantity of blood which they receive is enormous. Unless the function of these organs be disturbed, the blood passing through them cannot be deoxygenated, and is consequently red, containing a large quantity of oxygen and a very small proportion of carbonic acid. This fact we have often noted, and it has been observed by all who have examined the renal veins in living animals. In comparative analyses for gases of the blood of the renal artery and vein, Bernard found, in one examination, no carbonic acid in either specimen; the proportion of oxygen being twelve parts per hundred in volume for the artery, and ten parts for the vein. These observations were made at a temperature of from 50° to 53° Fahr. Making the analyses at about the temperature of the body, 104° to 113°, the quantity of carbonic acid was three parts for the artery and 3·13 parts for the vein; and the proportion of oxygen was 19·46 parts for the artery and 17·26 parts for the vein. When the secretion of urine was arrested by irritation of the kidney, the blood became black in the vein, and the quantity of oxygen diminished, with a corresponding increase in the proportion of carbonic acid.[4]

These observations show that during secretion most of

[1] SIMON, *Animal Chemistry*, Philadelphia, 1846, p. 178.

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 319.

[3] See page 21.

[4] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 160.

the blood sent to the kidneys is for the purpose of furnishing water and the excrementitious principles of the urine, and but little is used for ordinary nutrition. Secretion appears to have no marked influence upon the consumption of oxygen and the production of carbonic acid.

Physiological Anatomy of the Urinary Passages.—The chief physiological interest attached to the anatomy of the urinary passages is connected with the discharge of the urine from the kidneys into the bladder, and the process of micturition; and it will be necessary, consequently, to give but a brief account of the structure of these parts.

The excretory ducts of the kidneys, the ureters, commence each by a funnel-shaped sac, the pelvis, which is applied to the kidney at the hilum. This sac presents little tubular processes, called calices, into which the apices of the pyramids are received. The ureters themselves are membranous tubes of about the diameter of a goose-quill, becoming much reduced in caliber as they penetrate the coats of the bladder. They are from sixteen to eighteen inches in length, passing from the kidneys to the bladder behind the peritoneum. They have three distinct coats; an external coat, composed of fibrous tissue, the ordinary white fibres mixed with elastic fibres of the small variety; a middle coat, composed of different layers of non-striated muscular fibres; and a mucous coat.

The external coat requires no special description. It is continued into the calices and is continuous with the fibrous coat of the kidney at the apices of the pyramids.

The fibres of the muscular coat present two principal layers; an external longitudinal layer, and an internal transverse, or circular layer, to which is added near the bladder a layer of longitudinal fibres, internal to the circular fibres.

The mucous lining is thin, smooth, and without any follicular glands. It is thrown into slight longitudinal folds,

when the tube is flaccid, which are easily effaced by distention. The epithelium exists in several layers, and is remarkable for the irregular shape of the cells. They present, usually, numerous dark granulations, and one or two clear nuclei, with distinct nucleoli. Some of the cells are flattened, some are rounded, and some are caudate, with one or two prolongations.

Passing to the base of the bladder, the ureters become constricted, penetrate the coats of this organ obliquely, their course in its walls being a little less than one inch in length. This valvular opening allows the free passage of the urine from the ureters, but compression or distention of the bladder closes the orifices and renders a return of the fluid impossible.

The bladder, which serves as a reservoir for the urine, varies in its relations to the pelvic and abdominal organs as it is empty or more or less distended. When perfectly empty, it lies deeply in the pelvic cavity, and is then a small sac, of an irregularly-triangular form. As it becomes filled, it assumes a globular or ovoid form, rises up in the pelvic cavity, and, when excessively distended, may project into the abdomen. When the urine is voided at the normal intervals, the bladder, when filled, contains about a pint of liquid; but under pathological conditions, it may become distended so as to contain ten or twelve pints, and in some instances of obstruction, it has been found to contain even more. The bladder is usually more capacious in the female than in the male. It is held in place by certain ligaments and folds of the peritoneum, which it is unnecessary to describe in this connection, but which are so arranged as to allow of the various changes in volume and position which the organ is liable to assume under different degrees of distention.

The anatomy of the coats of the bladder possesses a certain amount of physiological interest. These are three in number. The external coat is simply a reflection of the

peritoneum, covering the posterior portion completely, from the openings of the ureters to the summit, about one-third of the lateral portion, and a small part of the anterior portion.

The middle, or muscular coat, consists of fibres of the non-striated or involuntary variety, arranged in three tolerably distinct layers.

The external muscular layer is composed of longitudinal fibres, which arise from parts adjacent to the neck, and pass anteriorly, posteriorly, and laterally over the organ, so that when they are contracted they diminish its capacity chiefly by shortening its vertical diameter. The anterior fibres of this layer arise from the body of the pubis and the symphysis by tendinous bands, known to most anatomists as the anterior ligaments. These tendinous fibres spread out on the prostate and are attached to its anterior surface. As the fibres on the anterior surface pass over the summit of the bladder, they interlace, and some of them are continuous with the fibres coming from the posterior surface. The posterior fibres arise from the base of the prostate, and, after forming a distinct band an inch or an inch and a quarter in breadth, spread out on the posterior surface of the bladder. The lateral fibres arise from the sides of the prostate and spread out upon the lateral surfaces of the bladder. In the female, the posterior fibres arise from the dense fibrous membrane between the neck of the bladder and the vagina, and the lateral fibres from the perineal aponeurosis, the anterior fibres arising from the pubis as in the male. The fibres of the external layer are of a pinkish hue, being much more highly colored than the other layers.

The middle muscular layer is formed of circular fibres, arranged, on the anterior surface of the bladder, in distinct bands at right angles to the superficial fibres. They are thinner and less strongly marked on the posterior and lateral surfaces.

The internal muscular layer is composed of excessively pale fibres arranged in longitudinal fasciculi, the anterior

and lateral bundles anastomosing with each other as they descend toward the neck of the bladder, by oblique bands of communication, and the posterior bundles interlacing in every direction, forming an irregular plexus. Here they are not to be distinguished from the fibres of the middle layer. This arrangement has given to these fibres the name of the plexiform layer, and it gives to the interior of the bladder its reticulated appearance. This layer is continuous with the muscular fibres of the urachus, the ureters, and the urethra.

The sphincter vesicæ is composed of a band of smooth fibres, about half an inch in breadth and one eighth of an inch in thickness, embracing the neck of the bladder and the posterior half of the prostatic portion of the urethra. The tonic contraction of these fibres prevents the flow of urine, and during the ejaculation of the seminal fluid, it offers an obstruction to its discharge into the bladder.

It is seen, from this arrangement of the muscular fibres of the bladder, that they are capable by their contraction of expelling the greatest part of the urine when the sphincter is relaxed.

The mucous membrane of the bladder is smooth, rather pale, thick, and loosely adherent to the submucous tissue, except over the corpus trigonum. The epithelium exists in several layers, and presents the same diversity in form that is observed in the pelvis of the kidney and the ureters; viz., the deeper cells are elongated and resemble the columnar epithelium, while the cells on the surface are flattened. In the neck and fundus of the bladder are a few mucous glands; some in the form of simple follicles, and others collected so as to form glands of the simple racemose variety.

The corpus trigonum is a triangular body, lying just beneath the mucous membrane at the base of the bladder, and extending from the urethra in front to the openings of the ureters. It is composed of white fibrous tissue, with a few elastic and muscular fibres. At the opening of the

urethra, it presents a small projecting fold of mucous membrane, which is sometimes called the uvula vesicæ. Over the whole of the surface of the trigone, the mucous membrane is very closely adherent, and is never thrown into folds, even when the bladder is entirely empty.

The blood-vessels going to the bladder are ultimately distributed to its mucous membrane. They are not very numerous, except at the fundus, where the mucous membrane is tolerably vascular. Lymphatics have been described as existing in the walls of the bladder, but Sappey, whose researches in the lymphatic system have been very extended and successful, has failed to demonstrate them in this situation.[1] The nerves of the bladder are derived from the hypogastric plexus.

The urethra is provided with muscular fibres and is lined by a mucous membrane, the anatomy of which will be more fully considered in connection with the function of generation. In the female the epithelium of the urethra is like that of the bladder. In the male the epithelial cells are small, pale, and of the columnar variety.

Mechanism of the Discharge of Urine.—In some of the lower orders of animals, in which the urine is of a semisolid consistence, the movement of vibratile cilia in the uriniferous tubes probably aids in the discharge of the urine; but in the human subject, the existence, even, of cilia is doubtful, and the urine is discharged into the pelvis of the kidneys and the ureters by pressure due to the act of separation of the fluid from the blood. Once discharged into the ureters, the course of the urine is determined in part by the *vis a tergo*, and in part, probably, by the action of the muscular coats of these canals. Müller has found that the ureters can be made to undergo a powerful local contraction upon the application of an intense galvanic current;[2] and Bernard has

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 516.
[2] MUELLER, *Manuel de physiologie*, Paris, 1851, tome i., p. 396.

shown that this may be produced by galvanization of the anterior root of the eleventh dorsal nerve.[1] Notwithstanding these facts, it is difficult to estimate the amount of influence ordinarily exerted by peristaltic contractions of the ureters; but when there is excessive accumulation of urine in the bladder, or when there is obstruction from any cause, such as the presence of a renal calculus, these contractions are probably quite energetic.

When the urine has accumulated to a certain extent in the bladder, a peculiar sensation is experienced which leads to the act for its expulsion. This desire to discharge the urine is probably due to the impression produced by the distention of the bladder, and is conveyed to the nervous centres through the sympathetic system. The intervals at which it is experienced are exceedingly variable. The urine is usually voided before retiring to rest and upon rising in the morning, and generally two or three times, in addition, during the day. It is dependent, however, very much upon habit, upon the quantity of liquids ingested, and upon the degree of activity of the skin; the latter conditions modifying the quantity of urine.

Evacuation of the bladder is accomplished by the muscular walls of the organ itself, aided by contractions of the diaphragm and the abdominal muscles and certain muscles which operate upon the urethra, and is accompanied by relaxation of the sphincter vesicæ. This act is at first voluntary, but once commenced, it may be continued by the involuntary contraction of the bladder alone. During the first part of the process, the distended bladder is compressed by the voluntary contraction of the diaphragm and the abdominal muscles; and this, after a time, excites the action of the bladder itself. A certain period usually elapses then before the urine begins to flow. When the bladder contracts, aided by the muscles of the abdomen and the dia-

[1] Unpublished lectures delivered by Bernard at the College of France in the Summer of 1861.

phragm, the resistance of the sphincter is overcome, and a jet of urine flows with considerable force from the urethra. All voluntary action may then cease for a time, and the bladder will nearly empty itself; but the force of the jet may at any time be considerably increased by voluntary effort.

It is a question whether the bladder be capable of entirely emptying itself by the action of its muscular walls. That almost all the urine may be expelled in this way in the human subject there can be no doubt; and it has been shown by experiments upon some of the inferior animals that the bladder may be completely evacuated when it has been removed from the abdominal cavity. This fact was observed long ago by Magendie in dogs.[1] In vivisections we have frequently observed the bladder so firmly contracted that it could contain hardly more than a few drops of liquid.

Toward the end of the expulsive act, when the quantity of liquid remaining in the bladder is slight, the diaphragm and the abdominal muscles are again called into action, and there is a convulsive, interrupted discharge of the small quantity of urine that remains. At this time the impulse from the bladder, and, indeed, the influence of the abdominal muscles and diaphragm, are very slight, and the flow of urine along the urethra is aided by the contractions of its muscular walls and the action of some of the perineal muscles, the most efficient being the accelerator urinæ; but with all this muscular action, a few drops of urine generally remain in the male urethra after the act of urination is accomplished. The process of evacuation of urine in the female is essentially the same as in the male, with the exception of the slight modifications due to differences in the direction and length of the urethra.

The movements of the bladder are regulated by the nervous system. According to the researches of Budge, the influence of the nervous system operates through the sympa-

[1] MAGENDIE, *Précis élémentaire de physiologie*, Paris, 1836, tome ii., p. 485.

thetic, and he has described a centre in the spinal cord, which presides over the contractions of the lower part of the intestinal canal, the bladder, and the vasa deferentia. This he calls the genito-spinal centre, and he has located it, in experiments upon rabbits, in the spinal cord opposite to the fourth lumbar vertebra. From this centre the nervous filaments pass through the sympathetic nerve which communicates with the ganglion corresponding to the fifth lumbar vertebra.[1] These experiments have been somewhat extended by M. Giannuzzi, who operated upon dogs. The location of a centre in the spinal cord somewhere in the lumbar region was confirmed, and it was further ascertained that certain filaments passed to the bladder from a point corresponding to the third lumbar vertebra, going through the mesenteric ganglia, to form part of the hypogastric plexus. Nervous filaments also passed directly to the bladder from a point in the spinal cord opposite the fifth lumbar vertebra. When the spinal cord at these points was irritated with the point of a needle, contraction of the muscular walls of the bladder was produced; but this result did not follow when the irritation was applied to the cord after division of the nerves above mentioned.[2]

[1] BUDGE, *Lehrbuch der speciellen Physiologie des Menschen*, Leipzig, 1862, S. 510.

[2] GIANNUZZI, *Recherches physiologiques sur les nerfs moteurs de la vessie.—Journal de la physiologie*, Paris, 1863, tome vi., p. 29.

CHAPTER VII.

PROPERTIES AND COMPOSITION OF THE URINE.

General physical properties of the urine—Quantity, specific gravity, and reaction—Composition of the urine—Urea—Origin of urea—Compounds of uric acid—Hippurates and lactates—Creatine and creatinine—Oxalate of lime—Xanthine—Fatty matters—Inorganic constituents of the urine—Chlorides—Sulphates—Phosphates—Coloring matter and mucus—Gases of the urine—Variations in the composition of the urine—Variations with age and sex—Variations at different seasons and at different periods of the day—Variations produced by food—Urina potus, urina cibi, and urina sanguinis—Influence of muscular exercise—Influence of mental exertion.

The importance of an exact knowledge of the properties and composition of the urine has long been recognized by physiologists; and our literature is full of observations, more or less valuable, upon this subject, dating from the discovery of urea by Hillaire Rouelle,[1] in the latter part of the last century, to the present time. It is impossible, however, to follow out in detail even the most important of the chemical researches upon the different urinary constituents, without exceeding the limits of pure human physiology; and the observations of the earlier authors, Scheele, Bergmann, Cruickshank,[2] Fourcroy, Vauquelin, Prout, and many others, have

[1] Milne-Edwards, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 395. This author gives a very full account of the earlier chemical researches into the composition of the urine, which resulted in a description of the properties of urea. The observations of Rouelle were quite imperfect; but the more elaborate researches of Scheele, Bergmann, and others, which will be cited farther on, gave a pretty correct idea of the chemical characters of this important excretion.

[2] Cruickshank was the first to describe the formation of crystals of the nitrate of urea. He added to the concentrated urine an equal bulk of nitrous (?)

now little more than an historical interest. But this can hardly be said of the analysis by Berzelius, made early in the present century; for even in recent authoritative works upon physiology, these are quoted as the most elaborate and reliable of the quantitative examinations of the renal excretion.[1] In treating of this subject, we propose to give simply the chemistry of the urine as it is understood at the present day, dwelling particularly upon its relations to the physiology of nutrition and disassimilation. In doing this it will be necessary to consider carefully the quantity, specific gravity, reaction, etc., of the urine, with the variations observed under different physiological conditions.

General Physical Properties of the Urine.—The color of the urine is very variable within the limits of health, depending chiefly upon the character of the food, the quantity of drink, and the activity of the skin. As a rule, the color is yellowish or amber, with more or less of a reddish tint. The fluid is perfectly transparent, free from viscidity, and exhales, when first passed, a peculiar aromatic odor, which is by no means disagreeable. Soon after the urine cools, it loses this peculiar odor, and has the odor known as urinous. This continues until the liquid begins to undergo decomposition. The color and odor of the urine are usually modified by the same physiological conditions. When the fluid contains a relatively large amount of solid matters, the color is more intense, and the urinous odor more penetrating; and when its quantity is increased by an excess of water, with the low specific gravity, the color is pale, and the odor faint. The urine passed in the morning is usually more intense in color than that passed during the day.

acid and an equal weight of water. This produced at first violent effervescence, and when cold, a large quantity of flat, shining crystals made their appearance. These crystals were undoubtedly nitrate of urea (CRUICKSHANK, *Experiments on Urine and Sugar*, in ROLLO, *Cases of the Diabetes Mellitus*, London, 1798, p. 441).

[1] BERZELIUS, *Suite du mémoire sur la composition des fluides animaux.—Annales de chimie*, Paris, 1814, tome lxxxix., p. 38.

It is somewhat difficult to measure the exact temperature of the urine at the moment of its emission. In some recent observations on this subject, by Dr. Byasson, in which a very delicate thermometer was used, and extraordinary care was taken to prevent any change in temperature before the estimate was made, the temperature, under physiological conditions, varied but a small fraction of a degree from 100° Fahr.[1] It is important to know the normal temperature of the urine, as it is liable to vary very considerably in certain diseases.

Quantity, Specific Gravity, and Reaction of the Urine. —In estimating the total quantity of urine discharged in the twenty-four hours, it is important to take into consideration the specific gravity, as an indication of the amount of solid matter excreted by the kidneys. We have already alluded to some of the variations in quantity constantly occurring in health, as depending upon the proportion of water; but the amount of solid matters excreted is usually more nearly uniform. It must also be taken into account that differences in climate, habits of life, etc., in different countries, have an important influence upon the daily quantity of urine. Dr. Parkes has collected the results of twenty-six series of observations made in America, England, France, and Germany, and finds the average daily quantity of urine in healthy male adults, between twenty and forty years of age, to be fifty-two and a half fluidounces, the average quantity per hour being two and one-tenth fluidounces. The extremes were thirty-five and eighty-one ounces.[2]

In attempting to decide the question whether a certain quantity of urine passed be abnormal or within the limits of health, it is important to recognize, if possible, certain limits of physiological variation. Becquerel states that the variations in the proportion of water in the urine likely to occur

[1] BYASSON, *Essai sur la relation qui existe à l'état physiologique entre l'activité cérébrale et la composition des urines*, Paris, 1868, p. 42, table.

[2] PARKES, *The Composition of the Urine*, London, 1860, p. 6.

in health are between twenty-seven and fifty fluidounces;[1] but his average of the total quantity in the twenty-four hours is only forty-four ounces, which is rather lower than the one we are disposed to adopt. The circumstances that lead to a diminution in the proportion of water are usually more efficient in their operation than those which tend to an increase; and the range below the healthy standard is rather wider than it is above. All these estimates, however, are merely approximative. Assuming that the usual quantity in the male is about fifty ounces, it may be stated, in general terms, that the range of normal variation is between thirty and sixty; and that when the quantity varies much from these figures, it is probably due to some pathological condition.

According to the researches of Becquerel, the quantity of water discharged by the kidneys in the twenty-four hours is a little greater in the female than in the male; but in the female the specific gravity is lower, and the amount of solid constituents is relatively and absolutely less.[2]

The specific gravity of the urine should always be estimated in connection with the absolute quantity in the twenty-four hours. Those who assume that the daily quantity is about fifty ounces give the ordinary specific gravity of the mixed urine of the twenty-four hours, at 60° Fahr., as about 1020. The specific gravity is liable to the same variations as the proportion of water, and the density is increased precisely as the amount of water is diminished. The ordinary range of variation in specific gravity is between 1015 and 1025; but without positively indicating any pathological condition, it may be as low as 1005, or as high as 1030.

The reaction of the urine is acid in the carnivora and alkaline in the herbivora. In the human subject it is usually acid at the moment of its discharge from the bladder; though at certain periods of the day it may be neutral or feebly

[1] BECQUEREL ET RODIER, *Traité de chimie pathologique appliquée à la médecine pratique*, Paris, 1854, p. 273.

[2] BECQUEREL ET RODIER, *op. cit.*, p. 270, table.

alkaline, depending upon the character of the food. The acidity may be measured by carefully neutralizing the urine with an alkali, in a solution that has previously been graduated with a solution of oxalic acid of known strength; and the degree of acidity is usually expressed by calling it equivalent to so many grains of crystallized oxalic acid.

As the result of numerous observations made by Vogel and under his direction, the total quantity of acid in the urine of the twenty-four hours in a healthy adult male is equal to from two to four grammes, or, omitting fractions, thirty to sixty grains of oxalic acid. The hourly quantity in these observations was equal, in round numbers, to from one and a half to three grains of acid. The proportion of acid was found to be very variable in the same person at different periods of the day. In one individual, upon whom the greatest number of observations was made, the average hourly quantity of acid at night was 2·9 grains; in the forenoon, 2 grains; and in the afternoon, 2·3 grains. "In a series of experiments made upon four different persons, the quantity was found to be greatest at night, least in the forenoon, and between these extremes in the afternoon."[1] The observations upon this subject by Prof. Dalton show that the variations noted by Vogel, in Germany, probably exist in this country, under the conditions of life met with in our large cities. Dr. Dalton found, in his own person, that the maximum of acidity was at night and in the early morning, the minimum being in the forenoon, and the mean in the afternoon and evening.[2]

In estimating the degree of acidity of the urine, it is necessary to test the fluid as soon as possible after it is discharged from the bladder; for its acidity rapidly increases after emission—until ammoniacal decomposition sets in—by the formation of organic acids, particularly the lactic.

[1] NEUBAUER AND VOGEL, *A Guide to the Qualitative and Quantitative Analysis of the Urine*, *The New Sydenham Society*, London, 1863, pp. 296, 389.

[2] DALTON, *A Treatise on Human Physiology*, Philadelphia, 1867, p. 335.

There has been considerable discussion and difference of opinion among physiological chemists with regard to the cause of the acid reaction of the urine. At the moment of its discharge from the bladder, it is distinctly, and even strongly acid; but it will not decompose the carbonates, like most acid solutions.[1] The weight of chemical authority upon this point is in favor of the view that there is no free acid in the urine when it is first passed, although the lactic acid, the acid lactates, and perhaps some other of the organic acids may be produced after emission, as the result of decomposition; but nearly all authors agree that it contains the acid phosphate of soda. The phosphates exist in the fluids of the body in at least three different conditions. The basic phosphate of soda, for example, possesses three atoms of the base, and has an alkaline reaction. In contact with carbonic acid, this salt may lose one atom of the base, forming the carbonate of soda and what is called the neutral phosphate, the latter, however, having a feebly alkaline reaction. In contact with uric acid, the neutral phosphate may lose still another atom of base, forming the urate of soda and the acid phosphate; and according to Neubauer and Vogel,[2] Robin,[3] and others, it is in this form that it exists in the urine, and the presence of this salt is the cause of its acidity. The acid phosphate of soda may or may not be associated, in the human subject, with the acid phosphate of lime, which ordinarily gives the intensely acid reaction to the urine of the carnivora.

Composition of the Urine.

Regarding the excrementitious constituents of the urine as a measure, to a certain extent, of the general process of disassimilation, it is probably more important to recognize the absolute quantity of these principles discharged in a

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 642.
[2] *Loc. cit.*
[3] *Op. cit.*, pp. 55, 293.

definite time than to learn simply their proportions in the urine; and in making out a table of the composition of the urine, we shall give, as far as possible, the absolute quantity of its different constituents excreted in twenty-four hours. This latter point, however, will be more elaborately considered in connection with the characters of the individual excrementitious principles and their variations under physiological conditions. In compiling this table, we have taken advantage of the elaborate bibliographical and experimental researches of Prof. Robin, contained in his recent work upon the humors,[1] but have made some changes and corrections in his list of urinary constituents:

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867. In the table given by Robin (p. 634), there is evidently a very serious error in one of the figures giving the proportion of water. In quotations from this table in a very recent French work on the chemistry of the urine, this error is corrected (BERGERET, *De l'urine*, Paris, 1868, pp. 13, 24).

Although this table represents, very nearly, the latest and most reliable observations upon the relative and absolute quantities of the urinary constituents, there are a few minor points that demand some explanation. For example, Robin estimates the proportion of hippurates at a little less than the proportion of urates, while many writers of high authority speak of the hippurates as excreted in rather larger quantity (PARKES, *The Composition of the Urine*, London, 1860, p. 13, and NEUBAUER AND VOGEL, *A Guide to the Qualitative and Quantitative Analysis of the Urine*, London, 1863, p. 33); but the investigations with regard to the daily excretion of hippuric acid have not been so definite and satisfactory as those on which the estimates of the excretion of uric acid are based. Robin gives, also, the proportion of creatine as 1·4 to 2·6 parts per 1,000, and of creatinine, 0·2 to 0·4 per 1,000; and most authors give in the urine a larger proportion of creatinine. This difference, however, is not important, for, as far as the process of excretion is concerned, these two substances may be regarded as a single principle; creatine being readily converted into creatinine in the urine by simple decomposition. In our endeavor to make this table as complete as possible, we have reduced the figures given by many authors to represent the amounts of uric acid, phosphoric acid, sulphuric acid, chlorine, etc., to the quantity of the salts as they actually exist. This is particularly important in a work on physiology, for chlorine and the various acids thus enumerated are not proximate constituents of the urine, except when combined with bases. It is simply a matter of convenience to estimate them separately, and the proportions of salts are readily calculated from the combining equivalents of the different elements.

Composition of the Human Urine.

Water (in 24 hours, 27 to 50 fluidounces—Becquerel)		967·47	to	940·36
Urea (in 24 hours, 355 to 463 grains—Robin)		15·00	"	23·00
Urate of soda, neutral and acid Urate of ammonia, neutral and acid (in small quantity) Urate of potassa (traces) Urate of lime (traces) Urate of magnesia (traces)	(In 24 hrs., 6 to 9 grs. of uric acid—Becquerel—or 9 to 14 grs. of urates, estimated as neut. urate of soda.)	1·00	"	1·60
Hippurate of soda Hippurate of potassa Hippurate of lime	(In 24 hrs., about 7·5 grs. of hippuric acid—Thudichum—equiv. to about 8·7 grs. of hippurate of soda.)	1·00	"	1·40
Lactate of soda Lactate of potassa Lactate of lime	(Daily quantity not estimated)	1·50	"	2·60
Creatine Creatinine	(In 24 hours, about 11·5 grains of both—Thudichum)	1·60	"	3·00
Oxalate of lime (daily quantity not estimated)		traces	"	1·10
Xanthine		not estimated.		
Margarine, oleine, and other fatty matters		0·10	to	0·20
Chloride of sodium (in 24 hours, about 154 grains—Robin)		3·00	"	8·00
Chloride of potassium		traces.		
Hydrochlorate of ammonia		1·50	to	2·20
Sulphate of soda Sulphate of potassa Sulphate of lime (traces)	(In 24 hrs., 23 to 38 grs. of sulphuric acid—Thudichum. About equal parts of sulphate of soda and sulphate of potassa—Robin—equiv. to from 22·5 to 37·5 grs. of each.)	3·00	"	7·00
Phosphate of soda, neutral Phosphate of soda, acid	(Daily quantity not estimated)	2·50	"	4·30
Phosphate of magnesia (in 24 hrs., 7·7 to 11·8 grs.—Neubauer)		0·50	"	1·00
Phosphate of lime, acid Phosphate of lime, basic	(In 24 hrs., 4·7 to 5·7 grs.—Neubauer)	0·20	"	1·30
Ammonio-magnesian phosphate (daily quantity not estim.)		1·50	"	2·40
(Daily excretion of phosphoric acid, about 56 grs.—Thudichum.)				
Silicic acid		0·03	"	0·04
Urrosacine Mucus from the bladder		0·10	"	0·50
		1,000·00		1,000·00

Gases of the Urine. (Parts per 1,000 in volume.)

Oxygen, in solution	0·82
Nitrogen, in solution. (Mean of fifteen observations—Morin)	9·59
Carbonic acid, in solution	19·62

Proportion of solid constituents, from 32·63 to 59·89 parts per 1,000.

Urea, $C_2H_4N_2O_2$.

As regards quantity, and probably as a measure of the activity of the general process of disassimilation, urea is the most important of the urinary constituents; and this substance, with the changes which it undergoes in the urine and the mode of its production in the system, has been most carefully studied by physiologists. Regarding the daily excretion of urea as a measure of nutritive force and physiological waste, its consideration would come properly under the head of nutrition, in connection with all other substances known to be the results of disassimilation; but it is more convenient to treat of its general physiological properties, and some of its variations in common with other excrementitious principles separated by the kidneys, in connection with the composition of the urine.

The formula for urea, showing the presence of a large proportion of nitrogen, would lead us to suppose that it is one of the products of the waste of the nitrogenized principles of the body. It is found, under normal conditions, in the urine, the lymph and chyle, the blood, the sweat, and the vitreous humor.[1] Its presence has lately been demonstrated also in the substance of the healthy liver in both carnivorous and herbivorous animals;[2] and it has farther been shown by Zalesky that it exists in minute quantity in the muscular juice.[3] Under pathological conditions, as has been already intimated, urea finds its way into various

[1] MILLON, *Présence de l'urée dans l'humeur vitrée de l'œil.—Annuaire de chimie*, Paris, 1848, p. 431. The discovery of urea in the vitreous humor was confirmed by Marchand and by Wöhler (Ibid., 1849, p. 540).

[2] The presence of urea in the substance of the liver in diseased conditions has frequently been observed, and lately its existence has been conclusively demonstrated in the healthy liver by Meissner. (*Beiträge zur Kenntniss des Stoffwechsels im thierischen Organismus.—Centralblatt für die medicinischen Wissenschaften*, 1868, No. 18, S. 275.)

[3] ZALESKY, *Untersuchungen über den Uraemischen Process*, Tübingen, 1865, Tabelle iii.

other fluids, such as the secretion from the stomach, the serous fluids, etc.

In connection with the chemical properties of urea, it is interesting to note that it is one of the few organic proximate principles that can be produced synthetically in the laboratory of the chemist.[1] As early as 1828, Wöhler obtained urea by adding sulphate of ammonia to a solution of cyanate of potassa.[2] The products of this combination are sulphate of potassa, with cyanic acid and ammonia in a form to constitute urea. The cyanate of ammonia is isomeric with urea, and the change is effected by a simple rearrangement of its elements, the formula being NH_4O,C_2NO (cyanate of ammonia), equivalent to $C_2H_4N_2O_2$ (urea). It has long been known that urea, in contact with certain animal substances, is readily convertible into carbonate of ammonia. This transformation is theoretically accomplished by adding to urea four atoms of water. $C_2H_4N_2O_2$ (urea) $+ 4\,HO = 2\,(NH_4O,CO_2)$. It has recently been stated by Kolbe, that when carbonate of ammonia is heated in sealed tubes to the temperature at which urea commences to decompose, it is converted into urea.[3] The decomposition of urea resulting in the carbonate of ammonia may be easily effected by various chemical means. As this occurs in the spontaneous decomposition of urea in the urine and elsewhere, it has been supposed that the symptoms of blood-poisoning following retention of the urinary constituents, in cases of disease of the kidneys, are due to the decomposition of the urea into carbonate of ammonia, and not to the presence of the urea itself in the blood. Many interesting experiments and observations have been made upon this subject, but it is now pretty generally admitted

[1] It is interesting, also, in this connection to refer to the synthesis of another of the organic proximate principles; viz., neurine, which has lately been accomplished by Wurtz (*Comptes rendus*, Paris, 1867, tome lxv., p. 1015).

[2] WÖHLER, *Sur la formation artificielle de l'urée.—Annales de chimie et de physique*, Paris, 1828, tome xxxvii., p. 330.

[3] *Journal of Anatomy and Physiology*, Cambridge and London, 1868, vol. ii., p. 430.

that the weight of evidence is against the carbonate-of-ammonia theory of uræmia.

Except as regards the probable changes that take place in the process of transformation of certain constituents of the tissues into urea, the chemical history of this substance does not present much physiological interest. Urea may be readily extracted from the urine, by processes fully described in all the modern works upon physiological chemistry; and its proportion may now be easily estimated by the new methods of volumetric analysis. It is not so easy, however, to separate it from the blood or the substance of any of the tissues, on account of the difficulty in getting rid of the other organic matters and the great facility with which it undergoes decomposition.

When perfectly pure, urea crystallizes in the form of long, four-sided, colorless, and transparent prisms, which are without odor, neutral, and in taste something like saltpetre. These crystals are very soluble in water and in alcohol, but are entirely insoluble in ether. In its behavior to reagents, urea acts as a base, combining readily with certain acids, particularly the nitric and oxalic. It also forms combinations with certain salts, such as the oxide of mercury, chloride of sodium, etc. It exists in the economy in a state of watery solution, with perhaps a small portion of it modified by the presence of chloride of sodium.

Origin of Urea.—There are two probable sources of urea in the economy, assuming that it always preëxists in the blood and is not formed in the kidneys. One of these is in the disassimilation of the nitrogenized constituents of the tissues, and the other in a transformation in the blood of an excess of the nitrogenized elements of food. Urea, as we have already seen, exists in considerable quantity in the lymph and chyle, and is found, also, in small proportion, in the blood. It has lately been detected in still smaller quantity in the muscular tissue;[1] but chemists have thus far been

[1] Zalesky, *loc. cit.* Meissner found urea in the muscles, liver, and brain,

unable to extract it from any other of the solid tissues, under normal conditions, except the substance of the liver. The fact that it exists in considerable quantity in the liver has led to the supposition that this is the organ chiefly concerned in its production.[1] With the small amount of positive information that we have upon this point, the view that the liver produces urea, while the kidneys are the organs chiefly concerned in its elimination, must be regarded as purely hypothetical. But if it be true that urea is the result of the physiological wear of the nitrogenized elements of the body, the liver would probably produce its share, in the ordinary process of disassimilation. The fact that urea has not yet been detected in normal muscular tissue is by no means a conclusive argument against its formation in this situation. We have lately shown that, although the liver is constantly producing sugar, none can be detected in its substance, for the reason that it is washed out as fast as it is formed, by the current of blood.[2] In the case of the muscles, it is by no means improbable that the lymph, and perhaps the blood, washes out the urea constantly, and keeps

in rabbits and dogs, after extirpation of the kidneys (*Bericht über Versuche der Urämie betreffend.—Zeitschrift für rationelle Medicin*, Leipzig u. Heidelberg, 1866, Dritte Reihe, Bd. xxvi., S. 232).

[1] MEISSNER, *Beiträge zur Kenntniss des Stoffwechsels im thierischen Organismus.—Centralblatt für die medicinischen Wissenschaften*, 1868, No. 18, S. 275. Meissner refers to Heynsius and Stokvis as having previously indicated, though in an imperfect manner, the presence of urea in the liver. Parkes states that when portions of the substance of the liver have been destroyed by disease, the urea is sometimes deficient in the urine, and that it has appeared to him that "the want of urea was in proportion to the amount of hepatic tissue destroyed" (*The Composition of the Urine*, London, 1860, p. 284).

[2] FLINT, Jr., *Experiments undertaken for the purpose of reconciling some of the Discordant Observations upon the Glycogenic Function of the Liver.—New York Medical Journal*, Jan., 1869, vol. viii., p. 373, *et seq.* The experiments detailed in this article we have since repeated in public demonstrations, and confirmed most fully. In our later observations, we showed absence of sugar in the blood from the portal vein and the substance of the liver, and the presence of a large quantity of sugar in the blood from the hepatic veins. The dog upon which these observations were made was in full digestion.

these parts free from its presence during normal conditions. In some late experiments by Meissner, in which the observations of Prévost and Dumas on the accumulation of urea in the blood of nephrotomized animals were confirmed, urea was found in dogs and rabbits, after removal of the kidneys, not only in the liver, but in the muscles and brain.[1]

Although our experimental knowledge does not warrant the unreserved conclusion that urea is produced primarily in the nitrogenized parts of the organism, particularly the muscular tissue, this view is exceedingly probable; and we must wait for farther information on this subject, until physiological chemists are able to follow out more closely the exact atomic changes that intervene between the functional operation of organized parts and the change of their substance into excrementitious matters.

When we come to consider the influence of food upon the composition of the urine, it will be seen that an excess of nitrogenized matter taken into the alimentary canal causes a proportionate increase in the quantity of urea discharged. This fact has led to the supposition that a part of the urea contained in the urine is the result of a direct transformation in the blood of the nitrogenized alimentary principles. This view must be regarded as purely hypothetical. We do not even know the nature of the process by which the nitrogenized elements of the tissues are transformed into excrementitious matter, and we are still more ignorant of the essential characters of nutrition proper. When more nitrogenized food is taken than is absolutely necessary, it is evident that the excess must be discharged from the system. This is never discharged in the same form in which it enters, like an excess of chloride of sodium or other inorganic matter, but it is well known that a series of complicated changes, called catalytic, are necessary, even before organic matters can be taken into the blood by absorption. There is no evi-

[1] MEISSNER, *Bericht über Versuche der Urämie betreffend.—Zeitschrift für rationelle Medicin*, Leipzig u. Heidelberg, 1866, Dritte Reihe, Bd. xxvi., S. 232.

dence of the direct transformation of these principles into urea before they have become part of the organized structures, except in a comparison of the proportions of nitrogen ingested and discharged; and this proves nothing with regard to the nature of the intermediate processes. At the present time, the most rational supposition is, that the nitrogenized elements of food nourish the corresponding constituents of the body, which are constantly undergoing conversion into excrementitious matters. Observations which have appeared to demonstrate the formation of urea directly from albuminoid substances have not been confirmed.[1]

There are certain arguments, based upon comparisons of the atomic constitution of urea with the elements of uric acid, creatine, and creatinine, in favor of the view that urea is the product of a higher degree of oxidation of the other excrementitious matters above-mentioned. It has been found, also, that urea may be formed artificially from uric acid, creatine, creatinine, xanthine, hypoxanthine, and some other bodies of similar nature.[2] That certain bodies are mutually convertible by the addition or subtraction of a few elements of water, there can be no doubt. Examples of these simple transformations are, the change of starch ($C_{12}H_{10}O_{10}$), dextrine, etc., into glucose ($C_{12}H_{14}O_{14}$); the change of creatine ($C_8H_9N_3O_4$) into creatinine ($C_8H_7N_3O_2$), etc.; but the atomic changes necessary for the conversion into urea of the principles from which this substance has been assumed to be produced are much more complicated. There is no positive proof that the proportion of these various principles in the muscles, blood, and urine, bears an inverse ratio to the proportion of urea. Again, the argument that the excrements of reptiles contain an excess of uric acid because the activity of oxidation is less than in the mammalia is met by the fact that in birds, where the amount of oxygen consumed is

[1] MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1862, tome vii., pp. 400, 401.

[2] NEUBAUER AND VOGEL, *op. cit.*, p. 9

greater, the proportion of urates is enormous; and urea is not generally found in this class, but is contained only in the excrements of the rapacious birds, and here only in small quantity.[1]

There are no sufficient reasons for regarding urea as the final result of oxidation of certain of the tissues of the body, uric acid, creatine, etc., being substances in an intermediate stage of transformation; and we are forced to admit that this principle is formed during the general process of disassimilation, probably from the nitrogenized elements of the body, by a destructive action, with the exact nature of which we are as yet imperfectly acquainted.

The daily amount of urea excreted is subject to very great variations. It is given in the table as ranging between 355 and 463 grains. This is much less than the estimates frequently given; but when the quantity has been very large, it has generally depended upon an unusual amount of exercise, of nitrogenized food, or the weight of the body has been above the average. Parkes gives the results of twenty-five different series of observations on this point. The lowest estimate is 286·1 grains, and the highest 688·4 grains.[2]

Compounds of Uric Acid.

Uric acid ($C_5HN_2O_2 + HO$) seldom, if ever, exists in a free state in the normal urine. It is exceedingly insoluble, requiring from fourteen to fifteen thousand times its volume of cold water, and from eighteen to nineteen hundred parts of boiling water for its solution.[3] It was at one time supposed to exist in the urine in sufficient quantity to give it its acid reaction; but it has since been ascertained that its solution does not redden litmus. Its presence in the urine uncombined must be regarded as a pathological condition; still, it is often

[1] Milne-Edwards, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 445.
[2] Parkes, *The Composition of the Urine*, London, 1860, p. 7.
[3] Neubauer and Vogel, *op. cit.*, p. 27.

found in urinary deposits, where it is interesting to study the peculiar and varied forms of its crystals. Frequently, in tables of the composition of the urine, the proportion of uric acid is given, but this is simply a matter of convenience, and has precisely the same signification as the estimates of the proportions of sulphuric or phosphoric acid. None of these acids constitute, of themselves, proximate principles of the urine, but are always combined with bases.

In normal urine, uric acid is combined with soda, ammonia, potassa, lime, and magnesia. Of these combinations, the urate of soda and the urate of ammonia are by far the most important and constitute the great proportion of the urates, the urates of potassa, lime, and magnesia existing only in minute traces. The urate of soda is very much more abundant than the urate of ammonia.[1] The union of uric acid with the bases is very feeble. If from any cause the urine become excessively acid after its emission, a deposit of uric acid is liable to occur. The addition of a very small quantity of almost any acid is sufficient to decompose the urates, when the uric acid appears after a few hours in a crystalline form.

Uric acid, probably in combination with bases, was found in the substance of the liver in large quantity by Cloetta;[2] and his observations have been confirmed by recent German authorities.[3] It is more than probable that the urates also exist in the blood and pass ready-formed into the urine; but their proportion in the blood is so slight under normal conditions, that their presence in this fluid has not been defi-

[1] The urates of soda exist in two forms; the neutral urate, in which there is one equivalent of the acid, and the acid urate, with two equivalents of acid. There are likewise neutral and acid urates of ammonia. The neutral salts exist in by far the larger quantity.

[2] CLOETTA, *De la présence de l'inosite, de l'acide urique, etc., dans diverses parties du corps animal.—Journal de la physiologie*, Paris, 1858, tome i., p. 802. Cloetta also noted the presence of uric acid in the substance of the spleen.

[3] MEISSNER, *op. cit.—Centralblatt für die medicinischen Wissenschaften*, 1868, No. 15, S. 226, *et seq.*

nitely determined, except in birds, where Meissner has lately found it in considerable quantity.[1] The fact that the urates exist in the liver, and in no other part—except, perhaps, the spleen—has led Meissner to the opinion that this organ is the principal seat of the formation of uric acid. However this may be—and the facts do not seem sufficiently definite to lead to such an exclusive opinion—it is certainly not formed in the kidneys, but is simply separated by these organs from the blood. Meissner did not succeed in finding uric acid in the muscular tissue, though the specimens were taken from the same animals in which he had found large quantities in the liver.

We have already discussed the theory of the change of uric acid into urea. In the present state of our knowledge, we must regard the urates, particularly the urate of soda, as among the products of disassimilation of the nitrogenized constituents of the body; and we should admit that as yet we are unable to designate the precise seat of their formation, or to follow out all the processes involved in their production.

The daily excretion of uric acid, given in the table, is from six to nine grains; which is equal to from nine to fourteen grains of urates estimated as neutral urate of soda. Like urea, the proportion of the urates in the urine is subject to certain physiological variations, which will be considered farther on.

Hippurates and Lactates.

The compounds of hippuric acid ($C_{18}H_8NO_5$), which are so abundant in the urine of the herbivora, are now known to be constant constituents of the human urine. Robin states that hippuric acid is always to be found in the urine of children, but that it is sometimes absent temporarily in the adult.[2] The presence of this acid in the normal human

[1] *Loc. cit.* [2] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 678.

urine seems to have been first established by Liebig;[1] and his researches have since been confirmed by numerous other observers. Lehmann, particularly, has been able to find this acid in his own urine, not only when on a purely vegetable diet, but during the use of a mixed diet. He is of the opinion that this principle frequently escapes observation when the urine has been evaporated too rapidly.[2]

The hippurates have been detected in the blood of the ox by Verdeil and Dolfuss,[3] and have since been found in the blood of the human subject;[4] and there can be scarcely any doubt that they pass, ready-formed, from the blood into the urine. With regard to the exact mode of origin of the hippurates, we have even less information than upon the origin of the other urinary constituents already considered. Experiments have shown that the proportion of hippuric acid in the urine is greatest after taking vegetable food; but it is found after a purely animal diet, and probably also exists during fasting. We must be content at present simply to class the hippurates among the products of disassimilation, without attempting to specify their exact mode of origin.[5] The daily excretion of hippuric acid amounts to about 7·5 grains;[6] equivalent to about 8·7 grains of hippurate of soda.

Hippuric acid itself, unlike uric acid, is quite soluble in water and in a mixture of hydrochloric acid. It requires six hundred parts of cold water for its solution, and a much less proportion of warm water. Under pathological conditions, it is sometimes found free in solution in the urine.

[1] LIEBIG, *Sur l'acide contenu dans l'urine des quadrupèdes herbivores.—Annales de chimie et de physique*, Paris, 1830, tome xliii., p. 188, *et seq.*

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol i., p. 179.

[3] ROBIN ET VERDEIL, *Chimie anatomique*, Paris, 1853, tome ii., p. 446.

[4] MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1857, tome i., p. 201.

[5] The reader is referred to works treating specially of the urine, for speculations concerning the origin and pathological relations of hippuric acid. An analysis of numerous observations on this subject has been made by Parkes. (*Composition of the Urine*, London, 1860, pp. 13, 29.)

[6] THUDICHUM, *A Treatise on the Pathology of the Urine*, London, 1858, p. 416.

The lactates of soda, potassa, and lime exist in very considerable proportion in the normal urine. They are undoubtedly derived immediately from the blood, passing, ready-formed, into the urine, where they exist in simple watery solution. According to Robin, the lactates are formed in the muscles, in the substance of which they can be readily detected.[1] We have no positive information with regard to the precise mode of formation of these salts. It is probable, however, that the lactic acid is the result of transformation of glucose. As a curious chemical fact, it is interesting to note that the lactic acid contained in the lactates extracted from the muscular substance is not absolutely identical with the acid resulting from the transformation of the sugars. The former have been called paralactates, and they contain one equivalent of water less than the ordinary lactates. According to Robin, the compounds of lactic acid in the urine are in the form of paralactates.[2]

Although the inosates (compounds of inosine, $C_{12}H_{12}O_{12}$) have never been detected in the urine, Robin is of the opinion that traces of these salts are separated from the blood by the kidneys, from the fact that they exist normally in the blood and in the muscular tissue.[3]

We have little or no information with regard to the relations of the inosates to excretion.

Creatine, $C_8H_9O_4N_3 + 2HO$, *and Creatinine*, $C_8H_7O_2N_3$.

Creatine and creatinine are undoubtedly identical in their relations to the general process of disassimilation, for one is easily converted into the other, out of the body, by very simple chemical means; and there is every reason to suppose that, in the organism, they are the products of physiological waste of the same tissue or tissues. These principles have been found in the urine, blood, muscular

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 681.
[2] *Loc. cit.* [3] *Loc. cit.*

tissue, and brain.[1] Scherer has demonstrated the presence of creatine in the amniotic fluid.[2] By certain chemical manipulations, both creatine and creatinine may be changed into urea; and the fact that these substances are now known to be constant constituents of the urine leaves no doubt that they are to be classed among the excrementitious principles. Chevreul, who first discovered creatine in the extract of muscular tissue, regarded it as one of the nutritive principles of meat;[3] but the subsequent researches of Heintz,[4] Liebig,[5] and others, who found it in the urine, revealed its true character. Verdeil and Marcet[6] have since found both creatine and creatinine in the blood; and these principles are now generally regarded as excrementitious matters, taken from the tissues by the blood, to be eliminated by the kidneys.

Creatine has a bitter taste, is quite soluble in cold water (one part in seventy-five), and is much more soluble in hot water, from which it separates in a crystalline form on cooling. It is but slightly soluble in alcohol, and is insoluble in ether. A watery solution of creatine is neutral. It does not readily form combinations as a base; but it has lately been made to form crystalline compounds with some of the strong mineral acids, the nitric, hydrochloric and sulphuric.[7] According to Neubauer and Vogel, when boiled for a long time with baryta, it is changed into urea and sar-

[1] VOIT, *Ueber das Verhalten des Kreatins, Kreatinins und Harnstoffs im Thierkörper.—Zeitschrift für Biologie*, München, 1868, Bd. iv., S. 78.

[2] SCHERER, *Analyse d'un liquide amniotique.—Annuaire de chimie*, Paris, 1850, p. 576.

[3] CHEVREUL, *Untersuchungen über die chemische Zusammensetzung der Fleischbrühe.—Journal für praktische Chemie*, Leipzig, 1835, Bd. vi., S. 120, *et seq.*

[4] HEINTZ, *Ueber eine neue Säure im menschlichen Harn.—Annalen der Physik und Chemie*, Leipzig, 1844, Bd. lxii., S. 602.

[5] LIEBIG, *Recherches de chimie médicale.—Comptes rendus*, Paris, 1847, tome xxiv., p. 69, *et seq.*

[6] ROBIN ET VERDEIL, *Traité de chimie anatomique*, Paris, 1853, tome ii., pp. 480, 489.

[7] NEUBAUER AND VOGEL, *op cit.*, p. 17.

cosine; but the recent researches of Voit have pretty conclusively shown that this change does not take place in the living organism, and that probably none of the urea of the urine is produced in this way.[1] When boiled with the strong acids, creatine ($C_8H_9O_4N_3 + 2HO$) loses four atoms of water, and is changed into creatinine ($C_8H_7O_2N_3$). This change takes place very readily in decomposing urine; which contains neither urea nor creatine, but a large quantity of creatinine, when far advanced in putrefaction.

Creatinine is more soluble than creatine, and its watery solution has a strong alkaline reaction. It is dissolved by eleven parts of cold water, and is even more soluble in boiling water. It is slightly soluble in ether, and is dis solved by one hundred parts of alcohol. This substance is regarded as one of the most powerful of the organic bases, readily forming crystalline combinations with a number of acids. According to Thudichum, who has very closely studied the physiological relations of these substances, creatine is the original excrementitious principle produced in the muscular substance, and creatinine is formed in the blood by a transformation of a portion of the creatine, somewhere between the muscles and the kidneys; "for, in the muscle, creatine has by far the preponderance over creatinine; in the urine, creatinine over creatine."[2]

In the present state of our knowledge, there is very little to be said with regard to the physiological relations of creatine and creatinine, except that they are probably to be classed among the excrementitious principles resulting from the disassimilation of the muscular tissue. As they exist in considerable quantity in the muscular substance, it becomes a question whether, in the urine of carnivorous animals, they be not derived from the food; but they could have no such origin in the herbivora, nor in the urine of

[1] VOIT, *Ueber das Verhalten des Kreatins, Kreatinins und Harnstoffs im Thierkörper.—Loc. cit.*, p. 116.

[2] THUDICHUM, *Pathology of the Urine*, London, 1858, p. 120.

starving animals. Thudichum mentions the fact that they are particularly abundant in the muscles of wild animals, and that the proportion diminishes in the same animals during captivity. He cites the instance of a fox that had been fed on meat for two hundred days at the Anatomical Institution in Giessen, in which the proportion of creatine was not one-tenth part that contained in the flesh of foxes caught by hunting.[1] It has likewise been found that the proportion of creatine is very small in fat meat.

It has been assumed by many authors that inasmuch as the muscular tissue of the heart is in almost constant action, it should contain more creatine than any other portion of the muscular system;[2] but the late observations on this point by Hofmann, Halenke, and Voit, show that the reverse of this is the case. These physiologists compared the proportion of creatine in the heart and in the muscles of the extremities, in oxen and in the human subject, and always found the quantity much less in the heart;[3] still the proportion of creatine has been found to be greater in tetanized muscles than in the muscular tissue after repose.

From the meagreness of our facts with regard to the physiological relations of creatine and creatinine, it is evident that there is much to be learned before we can understand the process of its formation in the healthy organism and the probable results of its retention or deficient elimination in disease. At present we can only say that these principles are probably produced in greatest part in the muscular tissue. The fact that creatine has lately been demonstrated in the brain would lead to the supposition that it is also one of the products of disassimilation of the nervous substance.

The average daily excretion of creatine and creatinine is estimated by Thudichum at about 11·5 grains. Of this he

[1] *Op. cit.*, p. 120.

[2] THUDICHUM, *loc. cit.*

— ROBIN ET VERDEIL, *Traité de chimie anatomique*, Paris, 1853, tome ii., p. 481.

[3] VOIT, *loc. cit.*, p. 84.

estimates that 4·5 grains consist of creatine, and 7 grains, creatinine.[1]

Oxalate of Lime, CaO,C_2O_3+2HO.

This salt is not constantly present in the normal human urine, though it may exist in considerable quantity without denoting any pathological condition. It is exceedingly insoluble, and the appearance of its crystals in urinary deposits is very characteristic. According to Robin, a trace may be retained in solution by the chlorides and the alkaline phosphates in the urine.[2] This salt may find its way out of the system by the kidneys, after it has been taken with vegetable food or with certain medicinal substances. The ordinary rhubarb, or pie-plant, contains a large quantity of oxalate of lime, which, when this article is taken, will pass into the urine. It is probable, however, that a certain quantity of the oxalate may be formed in the organism. Pathologists now recognize a condition called oxaluria, characterized by the appearance of oxalate-of-lime crystals in the urinary sediments; and sometimes the quantity in the urine is so large, and its presence is so constant, that it forms vesical calculi of considerable size.

Inasmuch as pathological facts have shown pretty conclusively that oxalic acid may appear in the system without being introduced with the food, some physiologists have endeavored to show how it may originate from a change in certain other of the proximate principles from which it can be produced artificially out of the body. One of the substances from which oxalic acid can be thus formed is uric acid. It remains, however, to show that this may take place in the living organism. Woehler and Frerichs injected into the jugular vein of a dog a solution containing about twenty-three grains of urate of ammonia. In the urine, taken a

[1] THUDICHUM, *A Treatise on the Pathology of the Urine*, London, 1858, p. 416.

[2] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 674.

short time after, there was no deposit of uric acid, but there appeared numerous crystals of oxalate of lime. The same result followed in the human subject, on the administration of sixty-seven grains of urate of ammonia by the mouth.[1] These questions have more of a pathological than a physiological interest; for the quantity of oxalate of lime in the normal urine is insignificant, and this salt does not represent any of the well-known processes of disassimilation.

Xanthine ($C_{10}H_4N_4O_4$).—Traces of this substance have been found in the normal human urine, but its proportion has not been estimated, and we are as yet but imperfectly acquainted with its physiological relations. Under pathological conditions, it occasionally exists in sufficient quantity to form urinary calculi. It has been found in the liver, spleen, thymus, pancreas, muscles, and brain. It is insoluble in water, but is soluble in both acid and alkaline fluids. Hypoxanthine ($C_{10}H_4N_4O_2$) has never been found in normal urine, though it exists in the muscles, liver, spleen, and thymus. Leucine ($C_{12}H_{13}N_2O_4$) exists in the pancreas, salivary glands, thyroid, thymus, suprarenal capsules, lymphatic glands, liver, lungs, kidney, and gray substance of the brain. It has never been detected in the normal urine. The same remarks apply to tyrosine ($C_{18}H_{11}NO_6$), though it is not so extensively distributed in the economy, taurine ($C_4H_7NO_6S_2$), and cystine ($C_6H_6N_4O_4S_2$). The last two, however, contain sulphur, and may have peculiar physiological and pathological relations that we do not at present understand.

These various substances are mentioned, though some of them have not been demonstrated in the normal urine, for the reason that there is evidently much to be learned with regard to the various products of disassimilation as they are represented by the composition of the urine. While some

[1] WOEHLER UND FRERICHS, *Ueber die Veränderungen, welche namentlich organische Stoffe bei ihren Uebergange in den Harn erleiden.—Journal für praktische Chimie*, Leipzig, 1848, Bd. xliv., S. 65.

of these may not be actual proximate principles, but substances produced by the processes employed for their extraction, some, which have thus far been discovered only under pathological conditions, may yet be found in health, and they represent, perhaps, important physiological acts.[1]

Fatty Matter.—A certain quantity of fat and fatty acids are said to exist in the normal urine.[2] Their proportion, however, is small, and the mere fact of their presence, only, is of physiological interest.

Inorganic Constituents of the Urine.

It is by the kidneys that the greatest quantity and variety of inorganic principles are discharged from the organism; and it is probable that even now we are not acquainted with the exact proportion and condition of all the principles of this class contained in the urine. In all the processes of nutrition, it is found that the inorganic constituents of the blood and tissues accompany the organic matters in their various transformations, though they are themselves unchanged. In fact, the condition of union of the inorganic with the organic principles is so intimate, that they cannot be completely separated without incineration. In view of these facts, it is evident that a certain part, at least, of the inorganic salts of the urine is derived from the tissues, of which, in combination with organic matters, they have formed a constituent part. As the kidneys frequently eliminate from the blood foreign matters taken into the system, and are capable sometimes of throwing off an excess of the normal constituents which may be introduced into the circulation, it can be readily understood how a large proportion of some

[1] For farther information concerning these principles, the reader is referred to works treating of the pathology as well as the physiology of the urine. A succinct statement of our positive knowledge regarding the doubtful principles is given by Robin (*Leçons sur les humeurs*, Paris, 1867, p. 688, *et seq.*).

[2] Robin, *op. cit.*, p. 690.

of the inorganic matters of the urine is derived from the food.

From the fact that the inorganic matters discharged in the urine are generally the same as those introduced with the food, and that they vary in proportion with the constitution of the food, it is difficult to ascertain how far their presence and quantity in the urine represent the processes of disassimilation. One thing, however, is certain: that the organic constituents of the food, the blood, the tissues, and the urine, are never without inorganic matter in considerable variety; and it is more than probable that the presence of these salts in a tolerably definite proportion influences the processes of absorption and secretion and has an important bearing upon nutrition; but we are as yet so imperfectly acquainted with the processes of nutrition of the tissues, that we cannot follow out all the relations of the inorganic matters, first to nutrition, and afterward to disassimilation.

Chlorides.—Almost all of the chlorine in the urine is in the form of chloride of sodium; the amount of chloride of potassium being insignificant and not of any special physiological importance. It is unnecessary, in this connection, to describe the well-known properties of common salt; and the means for determining its presence and proportion in the urine are fully treated of in works upon physiological chemistry. All that we have to consider is its importance and significance as a urinary constituent.

By reference to the table of the composition of the urine, it is seen that the proportion of chloride of sodium is subject to very great variations, the range being from three to eight parts per thousand. This at once suggests the idea that the quantity excreted is dependent to a considerable extent upon the amount taken in with the food; and, indeed, it has been shown by numerous observations that this is the fact.[1] The

[1] THUDICHUM, *A Treatise on the Pathology of the Urine*, London, 1858, p. 162. —NEUBAUER AND VOGEL, *A Guide to the Qualitative and Quantitative Analysis of*

proportion of chloride of sodium in the blood seems to be tolerably constant; and any excess that may be introduced is thrown off chiefly by the kidneys. It has been shown conclusively that deprivation of common salt in the food after a time is followed by serious disturbances in the general process of nutrition; and it is an acknowledged fact that this proximate principle is a constituent of every tissue of the body, except the enamel of the teeth. As the chlorides are deposited with the organic matter in all the acts of nutrition, they are found to be eliminated constantly with the products of disassimilation of the nitrogenized parts, and their absence from the food does not completely arrest their discharge in the urine. According to Robin, by suppressing salt in the food, its daily excretion may be reduced to from thirty to forty-five grains, the normal quantity being from one hundred and fifty to one hundred and sixty grains. This quantity is less than the amount contained in the ingesta, and under these circumstances there is a gradual diminution in the nutritive activity. "This fact demonstrates the necessity of adding chloride of sodium to the food."[1] It is an interesting pathological fact, that in all acute febrile disorders, the proportion of chlorine in the urine rapidly diminishes, and is frequently reduced to one hundredth of the normal amount.[2] The quantity rapidly increases to the normal standard during convalescence. Most of the chlorides of the urine are in simple watery solution; but a certain proportion of the chloride of sodium exists in combination with urea.

The daily elimination of chloride of sodium is about one hundred and fifty-four grains (Robin). The great variations in its proportion in the urine under different conditions of alimentation, etc., will explain the differences in the estimates given by various authorities.

the Urine, *New Sydenham Society*, London, 1863, p. 396.—Robin, *Leçons sur les humeurs*, Paris, 1867, p. 662.

[1] Robin, *op. cit.*, p. 663.

[2] Neubauer and Vogel, *op. cit.*, p. 397.

Sulphates.—There is very little to be said regarding the sulphates, beyond the general statements concerning the inorganic principles of the urine. The proportion of these salts is here very much greater than in the blood, in which there exists only about 0·28 of a part per thousand. Inasmuch as the proportion in the urine is from three to seven parts per thousand, it seems probable that the kidneys eliminate these principles as fast as they find their way into the circulating fluid either from the food or from the tissues.[1] Like other principles derived in great part from the food, the normal variations in the proportion of sulphates in the urine are very great. It is unnecessary to consider in detail the variations in the amount of sulphates discharged in the urine, depending upon the ingestion of different salts or upon diet, for all the recorded observations have been followed by the same results, and show that the ingestion of sulphates in quantity is followed by a corresponding increase in the proportion eliminated. Numerous experiments on this point have been made by Vogel and others.[2]

Thudichum estimates the daily excretion of sulphuric acid at from twenty-three to thirty-eight grains.[3] Assuming, with Robin, that the sulphates consist of about equal parts of sulphate of potassa and sulphate of soda, with traces of sulphate of lime,[4] the quantity of salts would be from 22·5 to 37·5 grains of sulphate of potassa and an equal quantity of sulphate of soda.

Phosphates.—The urine contains phosphates in a variety of forms; but inasmuch as it is not known that any one of the different combinations possesses peculiar relations to the process of disassimilation, as distinguished from the other phosphates, the phosphatic salts may be considered together.

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 663.
[2] NEUBAUER AND VOGEL, *op. cit.*, p. 404.
[3] THUDICHUM, *A Treatise on the Pathology of the Urine*, London, 1858, p. 416.
[4] ROBIN, *loc. cit.*

The remarks which we have just made with regard to the chlorides and the sulphates are applicable, to a certain extent, to the phosphates. These salts exist constantly in the urine, and are derived in part from the food, and in part from the tissues. Like other inorganic matters, they are united with the nitrogenized elements of the organism, and when these are changed into excrementitious principles, and are separated from the blood by the kidneys, they pass with them and are discharged from the organism.

It becomes a question of importance, now, to consider how far the phosphates are derived from the tissues, and what proportion comes directly from the food. This point is peculiarly interesting, from the fact that phosphorus has been shown to exist in the nerve-tissue, and it has been inferred that the excretion of phosphates represents, to some extent, the physiological wear of the nervous system.

All observers agree that the quantity of phosphates in the urine is in direct relation to the proportion in the food, and that an excess of phosphates taken into the stomach is immediately thrown off by the kidneys.[1] It is a familiar fact, indeed, that the phosphates are deficient and the carbonates predominate in the urine of the herbivora, while the reverse obtains in the carnivora; and that variations, in this respect, in the urine may be produced by feeding animals with different kinds of food. Verdeil made some very interesting comparative analyses of the blood for the alkaline phosphates in the herbivora, the carnivora, and in man. He found the proportion very small in the ox, as compared with the dog, and intermediate in the human subject. The proportion of phosphates in the blood of the dog was greatly diminished by feeding with potato.[2] Deprivation of food diminishes the quantity of phosphates in the urine, but a certain

[1] Neubauer and Vogel, *op. cit.*, p. 411. These observers found it impossible to establish any definite relation between the excretion of phosphoric acid and the processes of nutrition, in diseased conditions.

[2] Robin et Verdeil, *Chimie anatomique*, Paris, 1853, tome ii., p. 330.

proportion is discharged, derived exclusively from the tissues. We have already noted the fact that the products of disassimilation of the nitrogenized principles are never discharged in health without being accompanied with certain inorganic salts, such as the chlorides, sulphates, and phosphates.

In connection with the fact that phosphorus exists (in precisely what condition it is not known) in the nervous matter, it has been stated that mental exertion is always attended with an increase in the elimination of phosphates; and this has been advanced to show that these salts are specially derived from disassimilation of the brain-substance. Experiments show that it is not alone the phosphates that are increased in quantity under these conditions, but urea, the chlorides, sulphates, and inorganic matters generally;[1] and in point of fact, any physiological conditions which increase the proportion of nitrogenized excrementitious principles increase as well the elimination of inorganic matters. It cannot be assumed, therefore, that the discharge of phosphates is specially connected with the activity of the brain.[2] We learn nothing from pathology upon this point, for although numerous observations have been made upon the excretion of phosphoric acid in disease—Vogel having made about one thousand different analyses in various affections[3]—no definite results have been obtained.

From these facts it is seen that there is no physiological reason why we are able to connect the elimination of the phosphates with the disassimilation of any particular tissue or organ, especially as these salts in some form are universally distributed in the organism.

[1] This illustrates the combination of the organic principles with inorganic matter in excretion as well as in nutrition.

[2] BYASSON, *Essai sur la relation qui existe à l'état physiologique entre l'activité cérébrale et la composition des urines*, Paris, 1868, p. 66. By reference to the table by Byasson on p. 48, it will be seen that the proportion of sulphuric acid in the urine is more than doubled by mental exertion, while the proportion of phosphoric acid is increased less than one-third.

[3] NEUBAUER AND VOGEL, *op. cit.*, p. 413, *et seq.*

Observations have been made upon the hourly variations in the discharge of phosphoric acid at different periods of the day; but these do not appear to bear any absolute relation to known physiological conditions, not even to the process of digestion.[1]

Of the different phosphatic salts of the urine, the most important are those in which the acid is combined with soda. These exist in the form of the neutral and acid phosphates. The acid salt has one equivalent of the base, and is supposed to be the cause of the acidity of the urine at the moment of its emission. The so-called neutral salt is slightly alkaline, and has two equivalents of base. The proportion of the phosphates of soda in the urine is larger than that of any of the other phosphatic salts, but the daily amount excreted has not been estimated. The phosphate of magnesia is a constant constituent of the urine, as well as the acid and the basic phosphate of lime. The daily excretion of phosphate of magnesia amounts to from 7·7 to 11·8 grains, and of the phosphates of lime, from 4·7 to 5·7 grains.[2] According to Robin, there always exists in the urine a small quantity of the ammonio-magnesian phosphate, but it never, in health, exists in sufficient quantity to form a crystalline deposit.[3] The daily excretion of the phosphates is, as we have seen, subject to great variations, but the average quantity of phosphoric acid excreted daily may be estimated at about fifty grains, or, more accurately, fifty-six grains.[4]

The urine contains, in addition to the inorganic principles above described, a small quantity of silicic acid; but, as far as we know, this has no physiological importance.

[1] The reader is referred to the work of Neubauer and Vogel for a fuller consideration of the physiological and pathological relations of the phosphates.

[2] NEUBAUER AND VOGEL, *op. cit.*, p. 59.

[3] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 666.

[4] THUDICHUM, *A Treatise on the Pathology of the Urine*, London, 1858, p. 416.

Coloring Matter and Mucus.

The peculiar color of the urine is due to the presence of a nitrogenized principle, known to physiological chemists under a variety of names. We have mentioned it in the table as urrosacine. It is also called urochrome, urohæmatine, uroxanthine, and purpurine. We have no accurate account of its ultimate composition, and all that is known about its constituents is that it contains carbon, oxygen, hydrogen, and nitrogen, and probably iron.[1] Although its exact ultimate composition is not absolutely settled, its constituents are supposed to be the same as those of the coloring matter of the blood, the proportion of oxygen being very much greater. These facts point to the probability of the formation of urrosacine from hæmatine.

The quantity of coloring matter in the normal urine is very small. It is subject to considerable variation in disease, and almost always is fixed by deposits and calculi of uric acid or the urates, giving them their peculiar color. This principle first makes its appearance in the urine, and is probably formed in the kidneys. So little is known of its physiological or pathological relations to the organism, that it does not seem necessary to follow out all of the chemical details of its behavior in the presence of different reagents.

The normal urine always contains a small quantity of mucus, with more or less epithelium from the urinary passages, and a few leucocytes. These form a faint cloud in the lower strata of healthy urine, after a few hours' repose. The properties of the different kinds of mucus have already been considered.[2] An important peculiarity, however, of the mucus contained in normal urine is that it does not seem to excite decomposition of the urea, and that the urine may remain for a long time in the bladder without undergoing any putrefactive change.

[1] ROBIN ET VERDEIL, *Chimie anatomique*, Paris, 1853, tome iii., p. 398.

[2] See page 51.

Gases of the Urine.

In the process of separation of the urine from the blood by the kidneys, a certain proportion of the gases in solution in the circulating fluid is also removed. For a long time, indeed, it has been known that the normal human urine contained different gases, but lately some very interesting observations on this subject have been made by M. Morin,[1] in which the proportions of the free gases in solution have been accurately estimated. By using the method employed by Magnus in estimating the gases of the blood,[2] Morin was able to extract about two and a half volumes of gas from a hundred parts of urine. By careful experiments, he ascertained that a certain quantity of gas remained in the urine, and could not be extracted by his ordinary process. This amounted to about one-fifth of the whole volume of gas. Adding this to the quantity of gas extracted, he obtained the proportions to one litre of urine, in cubic centimetres, which are given in the table, viz.:

Oxygen	0·824
Nitrogen	0·589
Carbonic acid	19·620

These proportions represent the average of fifteen observations upon the urine secreted during the night.

The proportion of these gases was found by Morin to be subject to certain variations. For example, after the ingestion of a considerable quantity of water or any other liquid, the proportion of oxygen was considerably increased (from 0·824, to 1·024), and the carbonic acid was diminished more

[1] MORIN, *Recherches sur les gas libres de l'urine.—Journal de pharmacie et de chimie*, Paris, 1864, tome xlv., p. 396, *et seq.*

[2] The method of Magnus as applied to the gases of the urine does not involve the elements of inaccuracy which we have pointed out with reference to the blood (see vol. i., Respiration, p. 462); for in the urine there is no tendency to the disappearance of oxygen and the formation of carbonic acid, such as is due in the blood to the action of the corpuscles.

than one-half. The most interesting variations, however, were in connection with muscular exercise. After walking a long distance, the exercise being taken both before and after eating, the quantity of carbonic acid was found to be double that contained in the urine after repose. The proportion of oxygen was very slightly diminished, and the nitrogen was somewhat increased. The variations of these gases, however, were insignificant.

Morin explains the great increase in the proportion of carbonic acid, by the greater respiratory activity during exercise. It is well known, indeed, that muscular exercise largely increases the proportion of carbonic acid in the blood and the quantity eliminated by the lungs; and as the carbonic acid of the urine is undoubtedly derived from the blood, we should expect that the same conditions would increase its proportion in this secretion.

It is not probable that the kidneys are very important as eliminators of carbonic acid from the system, but it is certain that the presence of this gas in the urine assists in the solution of some of the saline constituents of this fluid, notably the phosphates.

Variations in the Composition of the Urine.

The urine represents in its varied constituents not only a great part of the physiological disintegration of the organism, but it contains elements evidently derived from the food. Its constitution is varying with every different condition of nutrition, with exercise, bodily and mental, with sleep, age, sex, diet, respiratory activity, the quantity of cutaneous exhalation, and, indeed, with every condition that affects any part of the system. There is no fluid in the body that contains such a variety of principles, as a constant condition, but in which the proportion of these principles is so variable. It is for this reason that we have given in the table of the composition of the urine the ordinary lim-

its of variation of its different constituents; and it has been found necessary, in treating of the individual excrementitious principles, to refer to some of the variations in their proportion in the urine. In treating more specially of the physiological variations of the urine, we shall only refer in general terms to conditions that produce wide and important changes in the proportion of its constituents; and under the head of nutrition, we shall consider how far the absolute quantities of the urinary principles and other excrementitious substances represent the physiological waste which is always coincident with the repair of parts. A full and complete history of all the variations in the urine would be inconsistent with the scope of this work.[1]

Variations with Age and Sex.—There are decided differences in the composition of the urine at different periods of life and in the sexes. These must depend in part upon the different conditions of nutrition and exercise, and in part upon differences in the food. Although the quantities of excrementitious matters present great variations, their relations to the organism are not materially modified, except, perhaps, at an early age; and the influence of sex and age is merely felt as they affect the diet and general habits of life.

It is stated by most authors that the urine of the fœtus is highly albuminous and contains no urea; but examinations of the urine in the fœtus and newly born have been so few that we know very little regarding its constitution and normal variations. The researches of the authorities on this subject, quoted by Parkes,[2] leave the question of the composition of the urine in the fœtus and during the first

[1] For more extended details of the variations of the urine in health and disease, the reader is referred to special treatises. Dr. Parkes considers these points very fully. (PARKES, *The Composition of the Urine in Health and Disease, and under the Action of Remedies*, London, 1859, pp. 39–179.)

[2] *Op. cit.*, p. 41, *et seq.*

days of extra uterine life still uncertain. In a specimen of urine taken from a still-born child delivered with forceps, examined by Drs. Elliot and Isaacs, the presence of urea was determined beyond a doubt. This urine was of a pale straw-color, like clear syrup in consistence, of an acid reaction, and a specific gravity of 1007·5. It contained neither sugar nor albumen. Well-marked crystals of the nitrate and of the oxalate of urea were obtained from this specimen.[1] Dr. Beale found urea in a specimen taken at the seventh month.[2]

With our present imperfect knowledge of the composition of the urine at the earliest periods of existence, it is impossible to deduce any conclusions regarding the production of the excrementitious principles at this time; and it would be unprofitable to detail the unsatisfactory and conflicting examinations to be found in works devoted specially to the urine.

Observations upon children between the ages of three and seven are more definite. At this period of life, the amount of urea excreted in proportion to the weight of the body is about double that in the adult. The amount of chlorine in children is about three times the quantity in the adult; and the proportionate amount of other solid matters is also greater. The amount of water excreted by the kidneys in children, in proportion to the weight of the body, is very much greater than in the adult, being more than double. From eight years of age to eighteen, the urinary excretion becomes gradually reduced to the adult standard.[3] It has been noticed by Gallois, that crystals of oxalate of lime are much more frequent in the urine of children between four and fourteen years of age than in the adult.[4]

[1] Elliot, *Urine in Fœtal Life.—American Journal of the Medical Sciences*, Philadelphia, 1857, New Series, vol. xxxiii., p. 555.

[2] Beale, *Kidney Diseases, Urinary Deposits, and Calculous Disorders*, Philadelphia, 1869, p. 125.

[3] Parkes, *op. cit.*, pp. 44, 45.

[4] Gallois, *De l'oxalate de chaux*, Paris, 1859, p. 14.

There are not many definite observations on record upon the composition of the urine in the latter periods of life. It has been shown, however, that there is a decided diminution, at this period, in the excretion of urea, and that the absolute quantity of the urine is somewhat smaller.

The absolute quantity of the urinary excretion in women is less than in men, and the same is true of the proportionate amount of these principles to the weight of the body; still, the differences in the proportionate excretion are not very marked, and the amount of all these principles being subject to modifications from the same causes as in men, the small deficiency, in the few direct observations upon record, may be in part, if not entirely, explained by the fact that women usually perform less mental and physical work than men, and that their digestive system is generally not so active.

Variations at Different Seasons, and at Different Periods of the Day.—The changes in the quantity and composition of the urine which may be directly referred to the conditions of digestion, temperature, sleep, exercise, etc., have long been recognized by physiologists; but it is difficult, if not impossible, so to separate these influences that the true modifying value of each can be fully appreciated. For example, there is nothing which produces such marked variations in the composition of the urine as the digestion of food. So marked, indeed, is its influence, that some writers of authority incline to the belief that the greatest part of what have been regarded as the most important excrementitious matters is derived from the food, and not from physiological disintegration of the tissues. Under strictly physiological conditions, the modifying influence of digestion must always complicate observations upon the effects of exercise, sleep, season, period of the day, etc.; and the urine is continually varying in health with the physiological modifications in the other processes and conditions of life. It will be sufficient for our purpo

to note the most important of these variations and endeavor to appreciate the conditions which combine to produce them, assigning to each one its proper value.

At different seasons of the year and in different climates, the urine presents certain variations in its quantity and composition. It seems necessary that a tolerably definite quantity of water should be discharged from the body at all times; and when the temperature or hygrometric condition of the atmosphere is favorable to the action of the skin, as in a warm, dry climate, the quantity of water in the urine is diminished, and its proportion of solid matters correspondingly increased. On the other hand, the reverse obtains when the action of the skin is diminished from any cause. This fact is a matter of common remark, as well as of scientific observation.

At different periods of the day, the urine presents constant and important variations. It is evident that the specific gravity must be constantly varying with the proportion of water and solid constituents. According to Dalton, the urine first discharged in the morning is dense and highly colored; that passed during the forenoon is pale and of a low specific gravity; and in the afternoon and evening it is again deeply colored, and its specific gravity is increased.[1] The acidity is also subject to tolerably definite diurnal variations, which have already been noted.[2]

Variations produced by Food.—An immense number of observations have been made upon the influence of ordinary food, and upon diet restricted to particular articles. These facts have necessarily been considered more or less fully in connection with the origin of the urinary constituents; but it is important, in studying the influence of muscular exercise, mental effort, etc., to constantly bear in mind the variations occurring under the influence of the ingesta.

[1] DALTON, *A Treatise on Human Physiology*, Philadelphia, 1867, p. 335.

[2] See page 190.

Water and liquids generally always increase the proportion of water in the urine and diminish the specific gravity. This is so marked after the ingestion of large quantities of liquids, that the urine passed under these conditions is sometimes spoken of by physiologists as the *urina potus*. This must be borne in mind in clinical examinations of the urine. It is a curious fact, however, that when an excess of water has been taken for purposes of experiment, the diet being carefully regulated, the absolute amount of solid matters excreted is considerably increased. This is particularly marked in the urea, but it is noticeable in the sulphates and phosphates, though not to any great extent in the chlorides. The results of experiments on this point seem to show that water taken in excess increases the activity of disassimilation.[1]

The ordinary meals invariably increase the solid constituents of the urine; the most constant and uniform increase being in the proportion of urea. This, however, depends to a great extent upon the kind of food taken. The increase is usually noted during the first hour after a meal, and attains its maximum at the third or fourth hour. The inorganic matters are increased, as well as the excrementitious principles proper. The urine passed after food has been called *urina cibi*, under the idea that it is to be distinguished from the urine supposed to be derived exclusively from disassimilation of the body, the *urina sanguinis*.

It is an interesting and important question to determine the influence of different kinds of food upon the composition of the urine, particularly the comparative effects of a nitrogenized and a non-nitrogenized diet. Lehmann has made some very striking observations upon this point, and his results have been fully confirmed by many other physiologists of authority. Without discussing elaborately all of these observations, it is sufficient to state that the ingestion of an excess of nitrogenized principles always produced a great increase in

[1] PARKES, *op. cit.*, p. 67, *et seq.*

the proportion of the nitrogenized constituents of the urine, particularly the urea. On a non-nitrogenized diet, the proportion of urea was found to be diminished more than one-half. The results of the experiments of Lehmann are so striking that we quote them in full:

"My experiments show that the amount of urea which is excreted is extremely dependent on the nature of the food which has been previously taken. On a purely animal diet, or on food very rich in nitrogen, there were often two-fifths more urea excreted than on a mixed diet; while, on a mixed diet, there was almost one-third more than on a purely vegetable diet; while, finally, on a non-nitrogenous diet, the amount of urea was less than half the quantity excreted during an ordinary mixed diet.

"In my experiments on the influence of various kinds of food on the animal organism, and especially on the urine, I arrived at the above results, which in mean numbers may be expressed as follows: On a well-regulated mixed diet I discharged, in twenty-four hours, 32·5 grammes of urea (I give the mean of fifteen observations); on a purely animal diet, 53·2 grammes (the mean of twelve observations); on a vegetable diet, 22·5 grammes (the mean of twelve observations); and on a non-nitrogenous diet, 15·4 grammes (the mean of three observations)."[1]

With regard to the influence of food upon the inorganic constituents of the urine, it may be stated in general terms that the ingestion of mineral substances increases their proportion in the excretions. We have already alluded to this fact in treating of the different inorganic salts.

There are certain articles which, when taken into the system, the diet being regular, seem to retard the process of

[1] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., pp. 150, 151.

These results are very important in their bearing upon the treatment of cases of structural disease of the kidneys; as they indicate how, by carefully regulating the diet, we may diminish the quantity of urea produced in the system, without affecting the general health.

disassimilation; or, at least, they diminish, in a marked manner, the amount of matters excreted, particularly the urea. Alcohol has a very decided influence of this kind. Its action may be modified by the presence of salts and other matters in the different alcoholic beverages, but in nearly all direct experiments, alcohol, either taken under normal conditions of diet, when the diet is deficient, or when it is in excess, diminishes the excretion of urea. The same is true of tea and coffee.[1]

Influence of Muscular Exercise.—There can be no doubt that muscular exercise, under ordinary conditions of diet, increases the proportion of many of the solid constituents of the urine, particularly the urea. It is impossible to come to any other conclusion, after studying the elaborate researches of Lehmann,[2] Liebig,[3] and others upon this subject. It must be remembered, in considering the effects of exercise upon the elimination of excrementitious matters, that the modifications in the urine produced by food are very considerable. We have purposely considered the influence of food before taking up other modifying conditions, so as to make apparent an important element of error in some recent observations, which are at variance with the prevailing ideas on this subject. When, for example, it has been shown that restriction to a non-nitrogenous diet will immediately diminish the daily elimination of urea more than one-half, it is evident that the diet must always be fully considered in experiments upon the effects of exercise or other modifying circumstances.

There is another important point, also, which is not always taken into consideration in comparative observations

[1] This subject has already been considered under the head of Alimentation. See vol. ii., Alimentation, p. 102, *et seq.*

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 151.

[3] LIEBIG, *The Source of Muscular Power.—The Pharmaceutical Journal and Transactions*, London, 1870, Third Series, part ii., p. 161, and part iii., pp. 181, 201, 221.

upon the absolute quantities of urea eliminated during exercise and repose, and that is the elimination of this principle by the cutaneous surface. We have already seen that urea is a constant constituent of the sweat. Speck, who found that exercise usually increased the elimination of excrementitious matters, noted the fact that urea was not increased in the urine when the sweat was very abundant.[1]

The very elaborate analysis of the principal observations on this subject by Parkes shows the discrepancies in the experiments of different authors, and points out several of the sources of error.[2] The weight of experimental evidence at that time was decidedly in favor of an increase in the elimination of urea by exercise; and the observations opposed to this view involved inaccuracies which would explain, in part at least, the contradictory results obtained. Lately, new observations have been made, which are assumed by some to show an actual diminution by exercise in the quantity of urea excreted. Fick and Wislicenus,[3] Frankland,[4] and Haughton[5] have attempted to show that this is

[1] SPECK, *Ueber die Wirkung der bis zur Ermüdung gesteigerten körperlichen Anstrengung unter verschiedenen Verhältnissen auf den Stoffwechsel.—Archiv zur Förderung der wissenschaftlichen Heilkunde*, Göttingen, 1860, Bd. iv., S. 591.

[2] PARKES, *The Composition of the Urine*, London, 1860, p. 85, *et seq.* Dr. Parkes has made some interesting observations, since the publication of his work on the urine, upon the influence of muscular exercise, under a non-nitrogenous diet, upon the elimination of urea. He found the amount of nitrogen in the excreta slightly increased over the amount eliminated during a period of rest, on the same diet. The elimination by the skin and intestines was taken into account in these experiments. PARKES, *On the Elimination of Nitrogen by the Kidneys and Intestines, during Rest and Exercise, on a Diet without Nitrogen.—Proceedings of the Royal Society*, London, 1867, vol. xv., No. 89, p. 339, *et seq.*

[3] FICK AND WISLICENUS, *On the Origin of Muscular Power.—London, Edinburgh and Dublin Philosophical Magazine*, London, Jan.–June, 1866, vol. xxxi., p. 485, *et seq.*

[4] FRANKLAND, *On the Origin of Muscular Power*, Ibid, July–Dec., 1866, vol. xxxii., p. 182, *et seq.*

[5] HAUGHTON, *Address on the Relation of Food to Work done by the Body, and its Bearing upon Medical Practice.—The Lancet*, London, Aug. 15, Aug. 22, and Aug. 29, 1868.

the fact, and have come to the conclusion that muscular force involves chiefly the consumption of non-nitrogenous principles and the production of carbonic acid. While the experiments on this subject have been so meagre, it would be unprofitable to enter into an elaborate discussion of their merits, particularly as they have not been directed specially to the influence of exercise upon the composition of the urine, but to the amount of muscular power developed by different kinds of food. This subject has not been reduced to such an absolute certainty that we are able to calculate mathematically the heat-units, the digestion-coefficients, and the amount of "work" produced by any given quantity of food; and such calculations cannot, as yet, take the place of actual experimental observations. What we want to know is the measurable influence of muscular exercise upon the proportion of certain of the constituents of the urine, under normal alimentation, every other modifying condition being taken into account. There can be no doubt that, with ordinary mixed diet, the elimination of urea is increased by exercise. Fick and Wislicenus made their observations, extending over a period of between one and two days, under a diet of non-nitrogenized matter; and Prof. Haughton compared his observations, made in July, with an average of experiments made at different seasons, taking no account of the action of the skin. It may be true that, with a purely non-nitrogenous diet, exercise fails to increase the quantity of urea eliminated by the kidneys, as appears from the observations of Fick and Wislicenus; but farther experiments are necessary to settle even this point; and recent observations by Parkes show that this is not always the case.[1]

With regard to the influence of muscular exercise upon the other constituents of the urine, experiments are somewhat contradictory. Sometimes the water is lessened, and sometimes it is increased; this probably depending upon the activity of the cutaneous exhalation. Sometimes the uric

[1] See page 227, note.

acid is increased, and sometimes diminished. The sulphates, phosphates, and chlorides are generally increased.

The general result of experimental observations on the effects of exercise upon the urine may be summed up in the proposition that this condition increases the activity of the nutritive processes, and produces a corresponding activity in the function of disassimilation, as indicated by the amount of excrementitious matters separated by the kidneys.[1]

Since the above has been written, we have had an opportunity of settling definitely the vexed question of the influence of muscular exercise upon the elimination of nitrogen.[2] In 1871, we made an exceedingly elaborate series of observations upon Mr. Weston, the pedestrian. Of these we can only give here a brief summary. Mr. Weston walked for five consecutive days as follows: First day, 92 miles; second day, 80 miles; third day, 57 miles; fourth day, 48 miles; fifth day, 40½ miles. The nitrogen of the food was compared with the nitrogen excreted for three periods; viz., five days before the walk, five days walking, and five days after the walk. A trusty assistant was with Mr. Weston day and night for the fifteen days; the food was weighed and analyzed; the excreta were collected; and other observations were made during the entire period. The analyses were made independently, under the direction of Prof. R. O.

[1] Dr. J. C. Draper made, in 1856, a number of observations upon the influence of exercise on the excretion of urea, from which he concluded that rest does not diminish this excretion, and that exercise does not increase, but actually lessens the quantity discharged. These conclusions are arrived at by comparing the amount of urea excreted by a patient confined to the bed with a fractured leg, with the average of eighteen observations upon other persons. The necessary experimental conditions are no better fulfilled in the other observations than in this, and the conclusions arrived at cannot therefore be accepted, in opposition to the accurate experiments of other observers (DRAPER, *Is Muscular Motion the Cause of the Production of Urea?—New York Journal of Medicine*, 1856, New Series, vol. xvi., p. 155, *et seq.*

[2] FLINT, JR., *On the Physiological Effects of Severe and Protracted Muscular Exercise, with Special Reference to its Influence upon the Excretion of Nitrogen.—New York Medical Journal*, 1871, vol. xiii., p. 609, *et seq.*

Doremus, who had no idea of the results until we had classified and tabulated them. The conclusions were most decided, and, as far as possible, all the physiological conditions were fulfilled. As regards the proportion of nitrogen eliminated to the nitrogen of the food, the general results were as follows:

For the five days before the walk, with an average exercise of about eight miles daily, the nitrogen eliminated was 95·53 parts for 100 parts of nitrogen ingested. For the five days of the walk, for every hundred parts of nitrogen ingested, there were discharged 174·81 parts. For the five days after the walk, when there was hardly any exercise, for every hundred parts of nitrogen ingested, there were discharged 91·93 parts. During the walk, the nitrogen excreted was in direct ratio to the amount of exercise; and, what was still more striking, the excess of nitrogen eliminated over the nitrogen of food almost exactly corresponded with a calculation of the nitrogen of the muscular tissue wasted, as estimated from the loss of weight of the body. Full details of the method of investigation, the processes employed, etc., are given in the original paper.

Influence of Mental Exertion.—Although the influence of mental exertion upon the composition of the urine has not been very much studied, the results of the investigations which have been made upon this subject are, in many regards, quite satisfactory. It is a matter of common remark that the secretion of urine is very often modified to a very great extent through the nervous system. Fear, anger, and various violent emotions sometimes produce a sudden and copious secretion of urine containing a large amount of water, and this phenomenon is very often observed in cases of hysteria. Very intense mental exertion will occasionally produce the same result. We have often observed a frequent desire to urinate during a few hours of intense and unremitting mental labor; and on one occasion being struck

with the amount of urine voided, it was found, on examination, to present scarcely any acidity and a specific gravity of about 1002. The interesting point in this connection, however, is to observe the influence of mental labor upon the elimination of solid matters, as contrasted with the amount of excretion during complete repose, the conditions of alimentation in the two instances being identical.

In a very interesting work upon the influence of cerebral activity upon the composition of the urine, Byasson found that by mental exertion the quantity of urine was increased; the amount of urea was also increased; the phosphoric acid was increased about one-third; the sulphuric acid was more than doubled; and the chlorine was nearly doubled.[1]

These facts have an important bearing upon our knowledge of the effects of mental exertion upon the process of disassimilation of the nervous tissue. They show that nearly all of the solid principles contained in the urine are increased in quantity by prolonged intellectual exertion, but they fail to point to any one excrementitious principle, either organic or inorganic, which is specially connected with the physiological wear of the brain. It has been assumed that elimination of the phosphates, increased out of proportion to the increase of the other solid matters of the urine, is one of the constant effects of intellectual effort; but this view is not sustained by direct physiological experiments, or by facts in pathology. We have already discussed this question somewhat elaborately, under the head of the phosphates of the urine.[2]

[1] Byasson, *Essai sur la relation qui existe à l'état physiologique entre l'activité cérébrale et la composition des urines*, Paris, 1868, p. 48, Table.

Thudichum (*Pathology of the Urine*, London, 1858, pp. 163, 164) noted a decided increase in the excrementitious constituents of the urine resulting from mental exertion.

[2] See p. 215.

CHAPTER VIII.

PHYSIOLOGICAL ANATOMY OF THE LIVER.

Coverings and ligaments of the liver—Capsule of Glisson—Lobules—Branches of the portal vein, the hepatic artery and duct—Interlobular vessels—Lobular vessels—Origin and course of the hepatic veins—Interlobular veins—Structure of a lobule of the liver—Hepatic cells—Arrangement of the bile-ducts in the lobules—Anatomy of the excretory biliary passages—Vasa aberrantia—Gall-bladder—Hepatic, cystic, and common ducts—Nerves and lymphatics of the liver—Mechanism of the secretion and discharge of bile—Secretion of bile from venous or arterial blood—Quantity of bile—Variations in the flow of the bile—Influence of the nervous system on the secretion of bile—Discharge of bile from the gall-bladder.

THE liver, by far the largest gland in the body, is now known to have several entirely distinct functions; and one of the most important of these has already been fully considered, in connection with digestion.[1] It is true that we know very little with regard to the exact office of the bile in digestion, but that this function is essential to life, there can be no doubt. We have, however, more positive information with regard to the excrementitious function of the liver and the changes which the blood undergoes in passing through its substance; and the study of these functions is closely connected with the anatomy of the liver and the chemical constitution of the bile.

Physiological Anatomy of the Liver.

It is unnecessary, in this connection, to dwell upon the ordinary descriptive anatomy of the liver. It is sufficient

[1] See vol. ii., Digestion, p. 360, *et seq.*

to state that it is situated just below the diaphragm, in the right hypochondriac region, and is the largest gland in the body, weighing, when moderately filled with blood, about four and a half pounds. Its weight is somewhat variable, but it is stated by Sappey that in a person of ordinary adipose development, its proportion to the weight of the body is about one to thirty.[1] In early life, the liver is relatively larger, its proportion to the weight of the body, in the newborn child, being as one to eighteen or twenty.[2]

The liver is covered externally by peritoneum, folds or duplicatures of this membrane being formed as it passes from the surface of the liver to the adjacent parts. These constitute four of the so-called ligaments that hold the liver in place. The proper coat of the liver is a very thin, but dense and resisting fibrous membrane, adherent to the substance of the organ, but detached without much difficulty, and very closely united to the peritoneum. This membrane is of variable thickness at different parts of the liver, being especially thin in the groove for the vena cava. At the transverse fissure it surrounds the duct, blood-vessels, and nerves, and penetrates the substance of the organ in the form of a vagina, or sheath, surrounding the vessels and branching with them. This membrane, as it ramifies in the substance of the liver, is called the capsule of Glisson. It will be more fully described in connection with the arrangement of the hepatic vessels.

The substance of the liver is made up of innumerable lobules, of an irregularly-ovoid or rounded form, and about $\frac{1}{25}$ of an inch in diameter. The space which separates these

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome ii., p. 261. Sappey made a number of examinations of the weight of the normal liver, with the vessels moderately distended with water, in order to represent, in a measure, its physiological condition. He estimated the weight from the average of ten livers, taken from both sexes and at different ages after adult life, at two kil., or about four and a half pounds. The weight of the liver with the vessels empty is about three and one-third pounds.

[2] WILSON, *Cyclopædia of Anatomy and Physiology*, London, 1839–47, vol. iii., p. 178, Article, *Liver*.

lobules is about one-quarter of the diameter of the lobule, and is occupied with the blood-vessels, nerves, and ramifications of the hepatic duct, all enclosed in the fibrous sheath. In a few animals, as, for example, the pig and the polar-bear, the division of the hepatic substance can be readily made out with the naked eye; but in man and in most of the mammalia, the lobules are not so distinct, though their arrangement is essentially the same. Although the lobules are intimately connected with each other from the fact that branches going to a number of different lobules are given off from the same interlobular vessels, they are sufficiently distinct to represent, each one, the general anatomy of the secreting substance of the liver; but before we study the minute structure of the lobules, it will be convenient to follow out the course of the vessels and the duct, after they have penetrated at the transverse fissure. In this description we will follow, in the main, the observations of Kiernan, who has given, probably, the most accurate account of the vascular arrangement in the liver.[1]

At the transverse fissure, the portal vein, collecting the blood from the abdominal organs, and the hepatic artery, a branch of the cœliac axis, penetrate the substance of the liver, with the hepatic duct, nerves, and lymphatics, all enveloped in the fibrous vagina, or sheath, known as the capsule of Glisson.[2] The portal vein is by far the larger of the two blood-vessels, and its caliber may be roughly estimated at from eight to ten times that of the artery.

The vagina, or capsule of Glisson, is composed of fibrous tissue, in the form of a dense membrane, closely adherent to the adjacent structure of the liver, and enveloping the vessels and nerves, to which it is attached by a loose areolar tissue. The attachment of the blood-vessels to the sheath is so loose, that the branches of the portal vein are collapsed when not filled with blood; presenting a striking contrast

[1] KIERNAN, *Philosophical Transactions*, London, 1833, p. 711, *et seq.*

[2] GLISSONIUS, *Anatomia Hepatis*, Amstelodami, 1665, p. 236.

to the hepatic veins, which are closely adherent to the substance of the liver, and remain open when they are cut across. This sheath is prolonged over the vessels as they branch and follows them in their subdivisions. It varies considerably in thickness in different animals. In man and the mammalia generally, it is rather thin, becoming more and more delicate as the vessels subdivide, and is entirely lost before the vessels are distributed in the interlobular spaces.

The vessels distributed in, and coming from the liver are the following:

1. The portal vein, the hepatic artery, and the hepatic duct, passing in at the transverse fissure, to be distributed in the lobules. The blood-vessels are continuous in the lobules with the radicles of the hepatic veins. The duct is to be followed to its branches of origin in the lobules.

2. The hepatic veins; vessels that originate in the lobules, and collect the blood distributed in their substance by branches of the portal vein and hepatic artery.

Branches of the Portal Vein, the Hepatic Artery and Duct.—These vessels follow out the branches of the capsule of Glisson, become smaller and smaller, and finally pass directly between the lobules. In their course, however, they send off lateral branches to the sheath; and those who follow exactly the description of Kiernan, call this the vaginal plexus. The arrangement of the vessels in the sheath is not in the form of a true anastomosing plexus, although branches pass from this so-called vaginal plexus between the lobules. These vessels, according to Sappey, do not anastomose or communicate with each other in the sheath.[1]

The portal vein does not present any important peculiarity in its course from the transverse fissure to the interlobular spaces. It subdivides, enclosed in its sheath, until its small branches go directly between the lobules, and in

[1] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, p. 288.

its course it sends branches to the sheath (vaginal vessels), which afterward go between the lobules. The distribution of the hepatic artery, however, is not so simple. This vessel has three sets of branches. As soon as it enters the sheath with the other vessels, it sends off minute branches (vasa vasorum), to the walls of the portal vein, the larger branches of the artery itself, the walls of the hepatic veins, and a very rich net-work of branches to the hepatic duct. When the hepatic artery is completely injected, the walls of the hepatic duct are seen almost covered with vessels. In its course, the hepatic artery also sends branches to the capsule of Glisson (capsular branches), which join with the branches of the portal vein to form the so-called vaginal plexus. From these vessels a few arterial branches are given off and pass between the lobules. The hepatic artery cannot be followed beyond the interlobular spaces. According to Kölliker and others, the terminal branches of the hepatic artery do not open into the radicles of the hepatic veins, but into small branches of the portal vein, within the capsule of Glisson.[1]

The hepatic duct follows the general course of the portal vein; but its structure and relations are so important and intricate that they will be described separately.

Interlobular Vessels.—Branches of the portal vein, coming from the terminal ramifications as the vessel branches within the capsule and the branches in the walls of the capsule, are distributed between the lobules, constituting the greatest part of the so-called interlobular plexus. These are situated between the lobules and surround them; each vessel, however, giving off branches to two or three lobules, and never to one alone. They do not anastomose, and consequently do not constitute a true plexus. The diameter of these interlobular vessels varies from $\frac{1}{1440}$ to $\frac{1}{720}$ of an inch.[2] In this distribution, the blood-vessels are followed

[1] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 443.

[2] KÖLLIKER, *op. cit.*, 1867, S. 441.

by branches of the duct, much less numerous and smaller, measuring only $\frac{1}{1500}$ of an inch; and some, even, have been measured that are not more than $\frac{1}{3000}$ of an inch in diameter.[1]

Lobular Vessels.—In the interlobular plexus, the ramifications of the hepatic artery are lost, and this can no longer be traced as a distinct vessel. One of the peculiarities of its arrangement, as we have seen, is that the artery does not empty into the radicles of the efferent vein, but joins the portal vessels as they are about to be distributed in a true capillary plexus in the substance of the lobules. In the lobules themselves, consequently, we have only to study the arrangement of the portal plexus, with the mode of origin of the hepatic veins and the relations of the hepatic duct.

The arrangement of the lobular plexus of blood-vessels is very simple. From the interlobular veins, a number of branches (eight to ten) are given off and penetrate the lobule. As the interlobular vessels are situated between different lobules, each one sends branches into two and sometimes three of these lobules; so that, as far as vascular supply is concerned, these divisions of the liver are never absolutely distinct.

After passing from the interlobular plexus into the lobules, the vessels immediately break up into a close network of capillaries, from $\frac{1}{3000}$ to $\frac{1}{2000}$ of an inch in diameter,[2] which occupy the lobules with a true plexus. These vessels are very numerous; and when they are fully distended by artificial injection, their diameter is greater than that of the intervascular spaces. It must be remembered, however, that in the study of the liver by minute injections, as in other parts, the vessels probably are distended so that they occupy more space than they ever do under the physiological conditions of the circulation. The blood, having been

[1] BEALE, *On some Points in the Anatomy of the Liver of Man and Vertebrate Animals*, London, 1856, p. 58.

[2] KÖLLIKER, *op. cit.*, 1867, S. 442.

distributed in the lobules by this lobular plexus, is collected by venous radicles of considerable size into a single central vessel in the long axis of the lobule, called the intralobular vein. A single lobule, surrounded with an interlobular vessel, showing the lobular capillary plexus, and the central vein (the intralobular vein) cut across, is represented in Fig. 9.

FIG. 9.

Transverse section of a single hepatic lobule. 1, Intralobular vein, cut across; 2, 2, 2, 2, Afferent branches of the intralobular vein; 3, 3, 3, 3, 3, 3, 3, 3, 3, interlobular branches of the portal vein—with its capillary branches, forming the lobular plexus, extending to the radicles of the intralobular vein. (SAPPEY, *Traité d'anatomie*, Paris, 1857, tome iii., p. 297.)

With regard to the mode of origin of the hepatic duct in the substance of the lobule, recent researches have shown that it begins by a very fine anastomosing plexus of vessels, with amorphous walls, situated between the liver-cells; but there are many different opinions on this subject, and we shall defer its full consideration until we take up the anatomy of the secreting structures in the lobules.

Origin and Course of the Hepatic Veins.—The blood distributed in the lobular capillary plexus furnishes the materials for the formation of bile, and undergoes those changes

produced by the action of the liver as a ductless gland; in other words, it is in and around this plexus that all the physiological functions of the liver are performed. It is then only necessary that the blood should be carried from the liver to go to the right side of the heart; and the arrangement of the hepatic veins is accordingly very simple.

Intralobular Veins.—The innumerable capillaries of the lobules converge into three or four venous radicles (represented in Fig. 9), which empty into a central vessel, from $\frac{1}{1000}$ to $\frac{1}{400}$ of an inch in diameter.[1] This is the intralobular vein. If a liver be carefully injected from the hepatic veins, and sections be made in various directions, it will be seen that the intralobular veins follow the long axis of the lobules, receiving vessels in their course, until they empty into a larger vessel, situated at what may be termed the base of the lobules. These vessels have been called, by Kiernan, the sublobular veins. They collect the blood in the manner just described from all parts of the liver, unite with others, becoming larger and larger, until finally they form the three hepatic veins, which discharge the blood from the liver into the vena cava ascendens.

The hepatic veins differ somewhat in their structure from other portions of the venous system. Their walls are thinner than those of the portal veins; they are not enclosed in a sheath, and are very closely adherent to the hepatic tissue. It is this provision which makes the force of respiration from the thorax so efficient in the circulation in the liver.[2] Here, indeed, a force added to the action of the heart is especially necessary; for the blood is passing in the liver through a second capillary plexus, having already been distributed in the capillaries of the alimentary canal and other abdominal organs, before it is received into the portal vein. It has also been noted that the hepatic veins possess a well-marked muscular tunic, very thin in man, but well-developed in the pig, the ox, and the horse, and composed

[1] KÖLLIKER, *op. cit.* 1867, S. 442.

[2] See vol. i., Circulation, p. 322.

of unstriped muscular fibres interlacing with each other in every direction.[1]

In addition to the blood-vessels just described, the liver receives venous blood from vessels which have been called accessory portal veins, coming from the gastro-hepatic omentum, the surface of the gall-bladder, the diaphragm, and the anterior abdominal walls. These vessels penetrate at different portions of the surface of the liver, and may serve as derivatives when the circulation through the portal vein is obstructed.

Structure of a Lobule of the Liver.—Each hepatic lobule, bounded and more or less distinctly separated from the others by the interlobular vessels, contains blood-vessels, radicles of the hepatic ducts, and the so-called hepatic cells. The arrangement of the blood-vessels has just been described; but in all preparations made by artificial injection, the space occupied by the blood-vessels is exaggerated by excessive distention, and the difficulties in the study of the relations of the ducts and the liver-cells are thereby much increased. Under any conditions, there are few questions, if any, in minute anatomy, that are so complicated as that of the origin of the bile-ducts in the lobules. If we were to attempt a critical analysis of the important investigations made upon this subject during the last thirty-five years, we should only illustrate the great diversity of opinion among eminent authors upon difficult anatomical questions. As the important problem in the minute anatomy of the lobules has been the relations of the cells to the radicles of the bile-ducts, we shall first take up the structure of the cells.

Hepatic Cells.—If a scraping from the cut surface of a fresh liver be examined with a moderately-high magnifying power, the field of view will be found filled with numerous rounded, ovoid, or irregularly-polygonal cells, measuring from $\frac{1}{1500}$ to $\frac{1}{1000}$ of an inch in diameter. In their natural con-

[1] SAPPEY, *op. cit.*, p. 300.

dition, they are more frequently ovoid than polygonal, and when they have the latter form, the corners are always rounded. These cells present one and sometimes two nuclei, sometimes with and sometimes without nucleoli. The presence of numerous small pigmentary granules gives to the cells a peculiar and characteristic appearance; and, in addition, nearly all of them contain a few granules or small globules of fat. Sometimes the fatty and pigmentary matter is so abundant as to obscure the nuclei. The addition of acetic acid renders the cells pale and the nuclei more distinct. By appropriate reagents, animal starch (probably glycogenic matter) has been demonstrated in the substance of the cells.[1]

Arrangement of the Bile-ducts in the Lobules.—Before the publication of the researches of Kiernan, no reasonable speculations, even, had been made with regard to the ultimate arrangement of the bile-ducts. Kiernan supposed that the lobules contained a reticulated net-work of ducts communicating with the ducts in the interlobular spaces; but he only inferred their existence, and his figures, which have been extensively copied, are merely diagrammatic.[2] The same arrangement essentially was described by Prof. Leidy, who figures a net-work of canals in the lobules, lined with the liver-cells; but the evidence in favor of this view is not convincing.[3] The results of the researches of Beale were at one time adopted by many anatomists. Beale supposed that there existed in the lobules delicate tubes, about as wide as the liver-cells, each tube enclosing a row of these cells.[4] The presence of this delicate membrane, however,

[1] SCHIFF, *De la nature des granulations qui remplissent les cellules hépatiques: Amidon animale.—Comptes rendus*, Paris, 1859, tome xlviii., p. 880.

[2] KIERNAN, *op. cit.—Philosophical Transactions*, London, 1833, p. 711, *et seq.*

[3] LEIDY, *Researches into the Comparative Structure of the Liver.—American Journal of the Medical Sciences*, Philadelphia, 1848, New Series, vol. xv., p. 13, *et seq.*

[4] BEALE, *On some Points in the Anatomy of the Liver of Man and Vertebrate Animals*, London, 1856, p. 73.

was not satisfactorily demonstrated. Kölliker formerly accepted in part the views advanced by Beale; but his ideas upon this subject, in all but the last edition of his work, have not been very definite.[1]

Such is the condition of the question of the origin of the biliary ducts, as it is understood by most English and American authors; and although the above statement does not represent all the views entertained by different anatomists, it is sufficient to show the exceedingly indefinite condition of the whole subject. Kölliker, indeed, in a letter to Dr. Sharpey, of London (1867), and in the last edition of his work on histology, abandons his former views, and states that he has become fully convinced of the accuracy of recent observations which lead to an entirely new description of the bile-ducts;[2] and Prof. Leidy, in his work on anatomy, published in 1861, does not commit himself to any definite opinion on the subject.[3] Late researches have shown that the following is probably the true relation of the ultimate ramifications of the bile-ducts in the lobules to the hepatic cells:

In the substance of the lobules is an exceedingly fine and regular net-work of vessels, of uniform size, about $\frac{1}{10000}$ of an inch in diameter,[4] which surround the liver-cells, each cell lying in a space bounded by inosculating branches of these canals. This plexus is entirely independent of the

[1] KÖLLIKER, *Manual of Human Microscopic Anatomy*, London, 1860, p. 346.

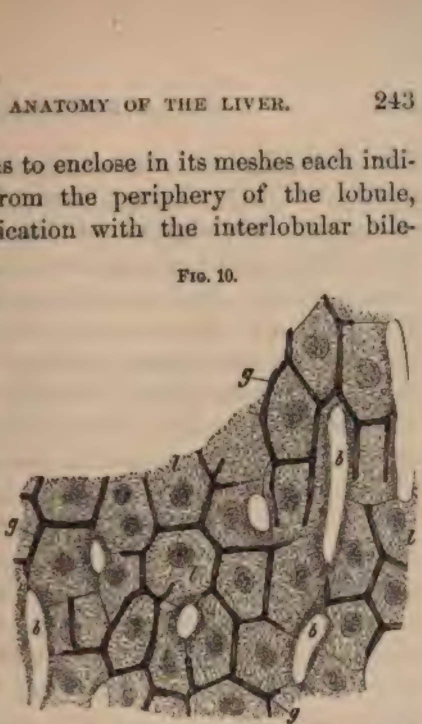
[2] *Journal of Anatomy and Physiology*, Cambridge and London, 1868, vol. ii., p. 163. These views have been adopted by Kölliker in the last edition of his work on Microscopic Anatomy (*Handbuch der Gewebelehre*, Leipzig, 1867, S. 428).

[3] LEIDY, *An Elementary Treatise on Human Anatomy*, Philadelphia, 1861, p. 327.

[4] This is the result of the measurements by Dr. Stiles (*Bulletin of the New York Academy of Medicine*, 1868, vol. iii., p. 351), of the ducts in the livers of the bullocks that died of the "Texas disease," which we have verified in the same specimen. The measurements given by Frey are about the same (*Handbuch der Histologie*, Leipzig, 1867, S. 558).

blood-vessels, and it seems to enclose in its meshes each individual cell, extending from the periphery of the lobule, where it is in communication with the interlobular bile-ducts, to the intralobular vein in the centre. The vessels probably have excessively thin, homogeneous walls—though the existence of their membrane has not been positively demonstrated—and are without any epithelial lining, being much smaller, indeed, than any epithelial cells with which we are acquainted. This arrangement, as far as is known, has no analogue in any other secreting organ.

FIG. 10.



Portion of a transverse section of an hepatic lobule of the rabbit, magnified 400 diameters. *b*, capillary blood-vessels; *g*, capillary bile-ducts; *l*, liver-cells. (KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 428.)

Although it is within three or four years only that the reticulated bile-ducts of the lobules have attracted much attention, they were discovered in the substance of the lobules, near the periphery, by Gerlach, in 1848.[1] It is evident, from an examination of his figures and description, that he succeeded in filling with injection that portion of the lobular network near the borders of the lobules, and demonstrated the continuity of their vessels with the interlobular ducts; but he did not recognize the vessels nearer the centre of the lobule. His views, however, received very little attention, and are not even mentioned in most of the authoritative works on general anatomy. Within the last

[1] GERLACH, *Handbuch der allgemeinen und speciellen Gewebelehre*, Mainz, 1848, S. 280, *et seq.*

few years, Budge,[1] Andrejevič,[2] Mac-Gillavry,[3] Chrzonszczewsky,[4] Wyss,[5] Hering,[6] Frey,[7] Eberth,[8] Kölliker,[9] and others have investigated this interesting question, by various methods, and have arrived at the most positive and satisfactory results. It is now demonstrated, beyond a doubt, that there are either canals or interspaces between the liver-cells in the lobules, and that these open into the interlobular hepatic ducts. It is still a question of discussion, whether these passages are simple spaces between the cells, or are lined by a membrane; but this point has no great physiological importance, and we can readily imagine that it would be exceedingly difficult to demonstrate a membrane forming the wall of a tube, the whole measuring but $\frac{1}{10000}$ of an inch. In the investigations which have thus demonstrated the arrangement of the finest bile-ducts in the lobules, the livers of rabbits have been found to present the most favorable conditions. It has been assumed, however, that in the method of study by artificial injection, the appearance of canals might be due to the extravasation of the fluid, which might possibly take on a regular arrangement between the cells. This is an error of observation that would not be unlikely to occur; but not only have these fine

[1] BUDGE, *Ueber den Verlauf der Gallengänge.—Archiv für Anatomie, Physiologie und wissenschaftlichen Medicin*, Leipzig, 1859, S. 642, *et seq.*

[2] ANDREJEVIČ, *Ueber den feineren Bau der Leber.—Sitzungsberichte der mathematisch-naturwissenschaftlichen Classe der Kaiserlichen Akademie der Wissenschaften*, Wein, 1861, Bd. xliii., I. Abtheilung, S. 379, *et seq.*

[3] MAC-GILLAVRY, *Zur Anatomie der Leber*, Idem, Wein, 1865, Bd. i., II. Abtheilung, S. 207, *et seq.*

[4] CHRZONSZCZEWSKY, *Zur Anatomie und Physiologie der Leber.*—VIRCHOW'S *Archiv*, Berlin, Jan., 1866, Bd. xxxv., S. 153, *et seq.*

[5] WYSS, *Beitrag zur Histologie der icterischen Leber.*—VIRCHOW'S *Archiv*, Berlin, April, 1866, Bd. xxxv., S. 553, *et seq.*

[6] HERING, *Ueber den Bau der Wirbelthierleber.—Sitzungberichte*, etc., Wein, 1866, Bd. liv., I. Abtheilung, S. 335.

[7] FREY, *Handbuch der Histologie*, Leipzig, 1867, S. 557, *et seq.*

[8] EBERTH, *Untersuchungen über die normale und pathologische Leber.*—VIRCHOW'S *Archiv*, Berlin, Mai, 1867, Bd. xxxix., S. 70, *et seq.*

[9] KÖLLIKER, *Handbuch der Gewebelehre*, Leipzig, 1867, S. 428.

ducts been filled by injection and their connection with the interlobular ducts apparently established, they have been observed filled with inspissated bile in icteric livers.[1] A method of study, very ingenious and highly satisfactory in its results, was adopted by Chrzonszczewsky. He introduced into the blood-vessels or stomach of a living animal a solution of indigo-carmine, and within one or two hours, killed the animal, when the whole net-work of ducts in the lobules was found unbroken and connected with the interlobular vessels. The drawings of these appearances accompanying the memoir are exceedingly beautiful.[2]

A peculiarly favorable opportunity for observing the bile-ducts in the lobules was presented in the livers of animals that died of the so-called "Texas cattle-disease." This was taken advantage of by Dr. R. C. Stiles, who was able to verify, in the most satisfactory manner, the facts which have lately been established by the German anatomists.[3] In these livers, the finest bile-ducts were found filled with bright yellow bile, and their relations to the liver-cells were beautifully distinct. In the examination of these specimens, the presence of what appeared to be detached fragments of these little canals is an argument in favor of the view that they were lined by a membrane of excessive tenuity. These interesting anatomical points were demonstrated by Dr. Stiles before the New York Academy of Medicine, and we have since been able to verify them in every particular.

Anatomy of the Excretory Biliary Passages.—There can be scarcely any doubt of the connection between the intercellular biliary plexus in the substance of the lobules and

[1] WYSS, *loc. cit.* [2] *Loc. cit.*

[3] STILES, *Bulletin of the New York Academy of Medicine*, 1868, vol. iii., p. 350; *Report of the New York State Cattle Commissioners, in connection with the Special Report of the Metropolitan Board of Health on the Texas Cattle-Disease.—Transactions of the New York State Agricultural Society*, Albany, 1868, vol. xxvii.—1867, Part ii., pp. 1137, 1160; and *Third Annual Report of the Metropolitan Board of Health of the State of New York*, Albany, 1868, p. 303.

interlobular ducts. We shall see, further on, that the cts, in their course from the lobules to the intestine, are ovided with numerous small racemose glands, which probbly secrete a mucus that is mixed with the bile; but, in all robability, the peculiar elements of the bile are formed in he lobules, and the canals situated between the lobules and leading from them to the larger ducts are merely excretory.

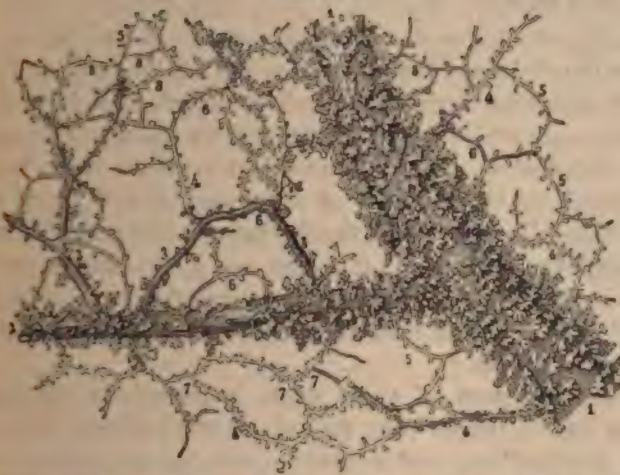
Between the lobules the ducts are very small, the smallest measuring about $\frac{1}{3000}$ of an inch in diameter. They are composed of a delicate membrane, lined with small, flattened epithelium. According to Robin, the cells lining the excretory ducts are ciliated;[1] but this is not the view generally adopted. The ducts larger than $\frac{1}{1200}$ of an inch have a fibrous coat, formed of inelastic, with a few elastic elements, and in the larger ducts there are, in addition, a few non-striated muscular fibres. The epithelium lining these ducts is of the columnar variety, the cells gradually undergoing a transition from the pavement form as the ducts increase in size. In the largest ducts there is a distinct mucous membrane, with mucous glands.

Throughout the whole extent of the biliary passages, from the interlobular canals to the ductus choledochus, are little utricular or racemose glands, varying in size in different portions of the liver, called, by Robin, the biliary acini. These are situated, at short intervals, by the sides of the canals. The glands connected with the smallest ducts are simple follicles, from $\frac{1}{800}$ to $\frac{1}{400}$ of an inch long. The larger glands are formed of groups of these follicles, and measure from $\frac{1}{250}$ to $\frac{1}{100}$ of an inch in diameter. The glands are only found connected with the ducts ramifying in the substance of the liver, and do not exist in the hepatic, cystic, and common ducts. They are composed of a homogeneous membrane, lined with small, pale cells of pavement-epithe-

[1] Littré et Robin, *Dictionnaire de médecine*, Paris, 1865, p. 611, Article, *Foie*.

lium. If the ducts in the substance of the liver be isolated, they are found covered with these little groups of follicles, and have the appearance of an ordinary racemose gland, except that the acini are relatively small and scattered. This appearance is represented in Fig. 11.

FIG. 11.



Anastomoses, and racemose glands attached to the biliary ducts of the pig, magnified eighteen diameters. 1, 1, Branch of an hepatic duct, with the surface almost entirely covered with racemose glands opening into its cavity; 2, branch in which the glands are smaller and less numerous; 3, 3, 3, branches of the duct with still simpler glands; 4, 4, 4, 4, biliary ducts with simple follicles attached; 5, 5, 5, 5, same with fewer follicles; 6, 6, 6, 6, 6, anastomoses in arches; 7, 7, 7, angular anastomoses; 8, 8, 8, 8, anastomoses by transverse branches. (SAPPEY, *Traité d'anatomie*, Paris, 1857, tome iii., p. 279.)

The excretory biliary ducts, from the interlobular vessels to the point of emergence of the hepatic duct, present numerous anastomoses with each other in their course.

Vasa Aberrantia.—In the livers of old persons, and occasionally in the adult, certain vessels are found ramifying on the surface of the liver, but always opening into the biliary ducts, which have been called vasa aberrantia. These are never found in the fœtus or in children. They are, undoubtedly, appendages of the excretory system of the liver, and are analogous in their structure to the ducts, but are

apparently hypertrophied, with thickened, fibrous walls, and present, in their course, irregular constrictions, not found in the normal ducts. The racemose glands attached to them are always very much atrophied. Sappey is of the opinion that these are ducts leading to lobules on the surface of the liver which have become atrophied.[1]

Gall-bladder, Hepatic, Cystic, and Common Ducts.—The hepatic duct is formed by the union of two ducts, one from the right and the other from the left lobe of the liver. It is about an inch and a half in length, and joins at an acute angle with the cystic duct, to form the ductus communis choledochus. The common duct is about three inches in length, of the diameter of a goose-quill, and opens into the descending portion of the duodenum. It passes obliquely through the coats of the intestine, and opens into its cavity in connection with the principal pancreatic duct. The cystic duct is about an inch in length and is the smallest of the three canals.

The structure of these ducts is essentially the same. They have a proper coat, formed of white fibrous tissue, a few elastic fibres, and a few non-striated muscular fibres. The muscular tissue is not sufficiently distinct to form a separate coat. The mucous membrane is always found tinged yellow with the bile, even in living animals. It is marked by numerous minute excavations, and is covered with cells of columnar epithelium. This membrane contains numerous mucous glands.

The gall-bladder is an ovoid or pear-shaped sac, about four inches in length, one inch in breadth at its widest portion, and capable of holding from an ounce to an ounce and a half of fluid. Its fundus is covered entirely with peritoneum, but this membrane passes only over the lower surface of the body.

The proper coat of the gall-bladder is composed of white fibrous tissue with a few elastic fibres. In some of the lower

[1] SAPPEY, *op. cit.*, tome iii., p. 283.

animals there is a distinct muscular coat, but a few scattered fibres only are found in the human subject. The mucous coat is of a yellowish color, and marked with numerous very small, interlacing folds, which are exceedingly vascular. Like the membrane of the ducts, the mucous lining of the gall-bladder is covered with columnar epithelium. In the gall-bladder are found numerous small racemose glands, formed of from four to eight follicles lodged in the submucous structure. These are essentially the same as the glands opening into the ducts in the substance of the liver, and secrete a mucus, which is mixed with the bile.

Nerves and Lymphatics of the Liver.—The nerves of the liver are derived from the pneumogastric, the phrenic, and the solar plexus of the sympathetic. The branches of the left pneumogastric penetrate with the portal vein, while the branches from the right pneumogastric, the phrenic, and the sympathetic surround the hepatic artery and the hepatic duct. All of these nerves penetrate at the transverse fissure and follow the blood-vessels in their distribution. They have not been traced farther than the terminal ramifications of the capsule of Glisson, and their exact mode of termination is unknown.

The lymphatics of the liver are very numerous. They are divided into two layers: the superficial layer, situated just beneath the serous membrane; and the deep layer, formed of a plexus surrounding the lobules and situated outside of the blood-vessels. The superficial lymphatics from the under surface of the liver, and that portion of the deep lymphatics which follows the hepatic veins out of the liver, pass through the diaphragm and are connected with the thoracic glands. Some of the lymphatics from the superior or convex surface join the deep vessels that emerge at the transverse fissure, and pass into glands below the diaphragm, while others pass into the thoracic cavity.

Mechanism of the Secretion and Discharge of Bile.—
e liver has no analogue in the glandular system, either in anatomy or its physiology. There is no gland in the onomy which we know to have two distinct functions, uch as the secretion of bile, and the production of certain elements destined to be taken up by the current of blood as it passes through. In other words, there is no organ in the body which has at the same time the functions of an ordinary secreting gland and a ductless gland. If we regard the liver-cells as the anatomical elements which produce the bile, it is evident that their number is very much out of proportion to the amount of bile secreted; and the liver itself is an organ of much greater size than it seems to us would be required for the mere secretion of bile. We explain this disproportionate size by the fact that the liver has other functions as a ductless gland.

There is no gland in which the arrangement of secreting tubes is the same as in the liver. It is hardly possible that the intercellular plexus of fine tubes in the lobules should be any thing but the plexus of origin, or the secreting portion of the hepatic duct. These are certainly not blood-vessels, and the only vessels that could have the appearance we have described, except the bile-ducts, are the lymphatics; but the communication between these vessels and the excretory bile-ducts, and the fact that they have been seen distended with bile in icteric livers, are pretty conclusive evidence of their nature. This arrangement, then, must be regarded as peculiar to the liver, as the arrangement of a capillary plexus, surrounded with cells and enveloped in a dilated extremity of a secreting tube, is peculiar to the kidney and is found in no other glandular organ.

Do the liver-cells, situated outside of the plexus of origin of the biliary duct, secrete the bile, which is taken up by these delicate vessels and carried to the excretory biliary passages? There are very good reasons for answering this question in the affirmative; though, if we do, we must recognize

the fact that the same cells produce glycogenic matter. As far as we are able to understand the mechanism of secretion, it seems necessary that a formed anatomical element, known as a secreting cell, should elaborate, from materials furnished by the blood, the elements of secretion; and this cannot be accomplished by a structureless membrane, like that which forms the walls of the bile-ducts.[1] Under this view, assuming that bile, as bile, first makes its appearance in these little lobular tubes, the liver-cells are the only anatomical elements capable of producing the secretion. With regard to the mechanism of this secreting action, we have nothing to say beyond our general remarks in the first chapter. With the view we have just expressed, certain elements of the bile are separated from the blood, and others are manufactured out of materials furnished by the blood by the liver-cells, and are taken up by the delicate plexus of vessels situated between the cells. The discharge of the fluid is like the discharge of any other of the secretions, except that a portion is temporarily retained in a diverticulum from the main duct, the gall-bladder.

The two distinct functions of the liver now recognized by many physiologists, namely, the secretion of bile and the formation of sugar, have led to the question of the existence in the liver of two anatomically distinct portions or organs, corresponding to its double physiological function. This view, indeed, has been advanced by several eminent anatomists. Robin recognizes two distinct parts in the liver; a biliary organ and a glycogenic organ. He regards the lobules, with their liver-cells and blood-vessels, as the parts concerned in the glycogenic function of the liver, and the little glands which open into the biliary ducts all along their course (see Fig. 11) and are arranged on the duct "in the form of leaves of fern," as the biliary

[1] An exception to this rule is in the secretion of milk during the period of greatest activity of the mammary glands. (See p. 79.)

organ.[1] The same independence of the glycogenic and biliary portions of the liver has been argued by others. Among the latest publications on this subject is a review of the question by Accolas;[2] but although this was published in 1867, there is no mention of the late researches, to which we have referred so fully, on the origin of the ducts in the lobules.

The fact of bile being found in the lobular canals and the demonstration of the direct communication of these canals with the excretory biliary ducts are powerful arguments in favor of the view that the bile is formed in the lobules, and probably by the liver-cells. What, then, is the function of the little acini connected exclusively with the biliary ducts? The similarity of their structure to that of the ordinary mucous glands, and to the mucous glands of the gall-bladder especially, would lead to the supposition that they secrete a mucous fluid. It is well known that the bile taken from the gall-bladder contains more mucus than that discharged directly from the liver; but the bile of the hepatic duct in most animals is somewhat viscid and contains a certain amount of mucus. This is the view entertained by Sappey, who states that the bile is viscid in different animals in proportion to the development of these little glands; and in the rabbit, in which the glands do not exist, the bile is remarkably fluid.[3]

Inasmuch as there is no direct evidence that the racemose glands attached to the excretory biliary passages have any thing to do with the secretion of the essential constituents of the bile, and as they are not even to be found in some animals that produce a considerable quantity of bile, we must regard the question of the isolation of two organs in

[1] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, p. 611, Article, *Foie*, and *Leçons sur les humeurs*, Paris, 1867, p. 551, *et seq.*

[2] ACCOLAS, *Essai sur l'origine des canalicules hépatiques et sur l'indépendance des appareils biliaire et glycogène du foie*, Strasbourg, 1867.

[3] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 280

the liver, one for the secretion of bile and the other for the production of sugar, as still unsettled. There is no evidence, indeed, that the bile is secreted anywhere but in the hepatic lobules.

Secretion of Bile from Venous or Arterial Blood.—Numerous experiments have been made with the view of determining whether the bile be secreted from the blood brought to the liver by the portal vein, or from the blood of the hepatic artery. The immense quantity of blood distributed in the liver by the portal vein led first to the opinion that the impurities were separated from this blood to form the bile, and that the hepatic artery had little or nothing to do with the secretion. This, indeed, was the view adopted by Glisson,[1] one of the earliest writers on the anatomy and functions of the liver. But since Bernard discovered the glycogenic function of the liver, this subject has assumed additional importance; and it becomes a question whether the materials for the secretion of bile may not be furnished by one vessel (the hepatic artery), while the other (the portal vein) is specially concerned in the formation of glycogenic matter. This theoretical view, however, is not carried out by well-established anatomical facts or by physiological experiments. It is not yet possible to separate the liver anatomically into two organs, one for the secretion of bile and the other for the production of sugar. It seems certain, also, from numerous experiments,[2] that bile may be secreted from the blood of the portal vein after a ligature has been applied to the hepatic artery; and it is equally certain, from the recent experiments of Oré,[3] that, if the portal vein be obliterated so gradually that the animal does not die from the operation, bile is secreted from the blood of the hepatic artery.

[1] GLISSONIUS, *Anatomia Hepatis*, London, 1654, p. 383.

[2] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 305.

[3] ORÉ, *Influence de l'oblitération de la veine porte sur la sécrétion de la bile.—Comptes rendus*, Paris, 1856, tome xliii., p. 463.

84

The experiments of M. Oré are very curious and instructive. After having repeatedly made the experiment of applying a tight ligature to the portal vein, producing thereby very grave symptoms and death so speedily that the effects upon the secretion of bile could not be satisfactorily observed, he modified his operations so as to effect a gradual obliteration of the vein. This he accomplished by simply applying a loose ligature, and tightening it from time to time until it came away. By this mode of procedure he succeeded in observing the secretion of bile six days or more after the application of the ligature; and, on killing the animals, he found the portal vein entirely obliterated and no communicating branches by which the blood could get from the portal system to the liver. From these observations it is concluded that the bile is secreted from the blood of the hepatic artery.

In support of this view, several instances of obliteration of the portal vein in the human subject are cited in works upon physiology. In a note to the communication of Oré in the *Comptes rendus*, Andral reports the case of a patient that died of dropsy, and on post-mortem examination the portal vein was found obliterated. In this instance the gall-bladder was found full of bile.[1] In addition, instances in which the portal vein emptied into the vena cava have been reported,[2] and in none was there any deficiency in the secretion of bile.

If the experiments upon the effects of tying the hepatic artery, and the observations of instances of obliteration of the portal vein and of congenital malformation, in which the portal vein does not go to the liver, be equally reliable, there

[1] *Comptes rendus*, Paris, 1856, tome xliii., p. 467.

[2] ABERNETHY, *Account of two Instances of Uncommon Formation, in the Viscera of the Human Body.—Philosophical Transactions*, London, 1793, p. 59.

—— LAWRENCE, *Account of a Child born without a Brain, which lived four Days; with a sketch of the principal deviations from the ordinary Formation of the Body; Remarks on their Production, and a view of some Physiological Inferences to which they lead.—Medico-Chirurgical Transactions*, London, 1814, vol. v., p. 174.

is but one conclusion to be drawn from them; and that is, that bile may be secreted from either venous or arterial blood. This view is not inconsistent with what we know of the general process of secretion and its applications to the production of bile. Regarding the bile as in part an excrementitious fluid, its effete element, cholesterine, is contained both in the blood of the portal vein and in the hepatic artery. Its recrementitious principles, glycocholates, taurocholates, etc., we suppose are produced *de novo* in the liver, out of materials furnished by the blood. The exact nature of the production of elements of secretion by glandular cells we do not understand; but there is no good reason to suppose that the principles necessary for the formation of bile may not be furnished by the blood of the portal vein, as well as by the hepatic artery.

The view most nearly in accordance with all the facts bearing on the question is, that bile is produced in the liver from the blood distributed in its substance by the portal vein and the hepatic artery, and not from either of these vessels exclusively; and that the bile may continue to be secreted, if either one of these vessels be obliterated, provided the supply of blood be sufficient.

Quantity of Bile.—The estimates of the daily quantity of bile in the human subject must be merely approximative; and our only ideas on this point are derived from experiments upon the inferior animals. The most complete and reliable observations on this subject are those of Bidder and Schmidt, and were made upon animals with a fistula into the gall-bladder, the ductus communis having been tied.[1] These observers found great variations in the daily quantity in different classes of animals, the quantity in the carnivora being the smallest. Applying their results to the human subject, assuming that the amount is about equal to the quantity secreted by the carnivora, the daily secretion in a man

[1] Bidder und Schmidt, *Die Verdauungssäfte*, Leipzig, 1852, S. 209.

weighing one hundred and forty pounds would be about two and a half pounds.[1]

Variations in the Flow of the Bile.—We have already considered, in another section, the variations in the flow of bile, and their relation to the process of intestinal digestion.[2] It is sufficient in this connection to repeat that the discharge from a biliary fistula in a dog increases immediately after eating; that it is at its maximum from the second to the eighth hour, during which time it does not vary to any great extent; after the eighth hour it begins to diminish, and from the twelfth hour to the time of feeding, it is at its minimum. Prof. Dalton made observations on the flow of bile from a fistula into the duodenum, which would represent the physiological discharge of bile into the intestine more nearly than observations with a biliary fistula. He found that by far the largest quantity passes into the intestines immediately after feeding and within the first hour.[3] These results agree in all essential particulars with previous observations on this subject, which have been very numerous; and they show that while the bile is discharged much more abundantly during intestinal digestion than during the intervals of digestion, its production and discharge are constant. This, we shall see in the next chapter, is a strong argument in favor of the view that the liver has an excrementitious function.

The bile is stored up in the gall-bladder to a considerable extent during the intervals of digestion. If an animal be killed at this time, the gall-bladder is always distended;

[1] This is the estimate adopted by Dalton (*Treatise on Human Physiology*, Philadelphia, 1867, p. 172). In our own experiments, made on a dog with a biliary fistula, the object was not so much to ascertain the entire quantity of bile in the twenty-four hours as to note the variations in its flow. The estimate was made in a dog that had become somewhat enfeebled, and is undoubtedly too low. (See vol. ii., Digestion, p. 375.)

[2] See vol. ii., Digestion, p. 375.

[3] Dalton, *op. cit.*, p. 176.

but it is found empty, or nearly so, in animals killed during digestion.

The influence of the nervous system upon the secretion of bile has been very little studied, and the question is one of great difficulty and obscurity. The liver is supplied very abundantly with nerves, both from the cerebro-spinal and the sympathetic system, and some observations have been made upon the influence of the nerves on its glycogenic function; but with regard to the secretion of bile, we can only apply our general remarks concerning the influence of the nervous system on secretion.[1]

The bile is discharged through the hepatic ducts like the secretion of any other gland. During digestion, the fluid accumulated in the gall-bladder passes into the ductus communis, in part by contractions of its walls, and in part, probably, by compression exerted by the distended and congested digestive organs adjacent to it. It seems that this fluid, which is necessarily produced by the liver without intermission, separating from the blood certain excrementitious matters, is retained in the gall-bladder for use during digestion.

[1] See page 28, *et seq.*

The extent of our knowledge of the influence of the nervous system on the secretion of bile is well presented in the following paragraph:

"The nervous system has assuredly a very great influence on the resorption of bile or on an obstacle offered to its discharge; but we know nothing distinct relative to this action, although we cannot deny it in the face of instances where fear has been sufficient to suddenly produce icterus. The cause of this can only be attributed to the influence of the pneumogastric or the grand sympathetic (BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 212).

CHAPTER IX.

EXCRETORY FUNCTION OF THE LIVER.

General properties of the bile—Composition of the bile—Biliary salts—Taurocholate of soda—Glycocholate of soda—Origin of the biliary salts—Cholesterine—Process for the extraction of cholesterine—Biliverdine—Tests for bile—Test for biliverdine—Test for the biliary salts—Pettenkofer's test—Excretory function of the liver—Origin of cholesterine—Experiments showing the passage of cholesterine into the blood as it circulates through the brain—Analyses of venous blood from the two sides of the body in cases of hemiplegia—Elimination of cholesterine by the liver—Analyses showing accumulation of cholesterine in the blood in certain cases of organic disease of the liver—Cholesteræmia.

ALTHOUGH the function of the bile in intestinal digestion is essential to life, we know very little of its mode of action; and we have thought proper to defer until now a full consideration of the properties and composition of this secretion. For an account of what is known of its digestive function, the reader is referred to the section of volume second, treating of digestion. We shall show, in this connection, that the liver excretes one of the most important of the effete principles; but before taking up the relations of the bile as an excretion, it will be necessary to study its general properties and composition.

General Properties of the Bile.—The secretion, as it comes directly from the liver, is somewhat viscid; but after it has passed into the gall-bladder, its viscidity is much greater from farther admixture of mucus.

The color of the bile is very variable within the limits

of health. It may be of any shade between a dark, yellowish-green and a reddish-brown. It is semitransparent, except when the color is very dark. In different classes of animals the variations in color are very great. In the pig it is bright-yellow; in the dog it is dark-brown; and in the ox it is greenish-yellow. As a rule, the bile is dark-green in the carnivora and greenish-yellow in the herbivora.

The specific gravity of the human bile, according to Prof. Dalton, is 1018;[1] but this is somewhat lower than the average usually given, which is from 1020 to 1026.[2] When the bile is perfectly fresh, it is almost inodorous, but it readily undergoes putrefactive changes. It has an excessively disagreeable and bitter taste. It is not coagulated by heat. When mixed with water and shaken, it becomes frothy, probably on account of the tenacious mucus and its saponaceous constituents.

It is generally stated that the bile is invariably alkaline. This is true of the fluid discharged from the hepatic duct,[3] although the alkalinity is not strongly marked; but the reaction varies after it has passed into the gall-bladder. Bernard found it sometimes acid and sometimes alkaline in the gall-bladder, in animals, dogs and rabbits, killed under various conditions;[4] but many of these animals were suffering from the effects of severe operations. In the hepatic ducts the reaction is always alkaline; and there are no observations on human bile that show that the fluid is not alkaline in all of the biliary passages.

We have already noted the fact that the epithelium of the biliary passages is strongly tinged with yellow, even in living animals. This is due to the remarkable facility with which the coloring principle of the bile stains the animal tissues. This is very well-illustrated in icterus, when even a

[1] DALTON, *Treatise on Human Physiology*, Philadelphia, 1867, p. 159.

[2] LONGET, *Traité de physiologie*, Paris, 1868, tome i., p. 278.

[3] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 538.

[4] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 212.

small quantity of this coloring matter finds its way into the circulation.

Perfectly normal and fresh bile, examined with the microscope, presents only a certain amount of mucus, the characters of which we have already described. There are no formed anatomical elements characteristic of this fluid. The fatty and coloring matters are in solution, and not in the form of globules or granules.

Composition of the Bile.

It is a remarkable fact, that although the bile, in a perfectly fresh and normal condition, may be obtained from the inferior animals with the greatest facility, no satisfactory analyses of its characteristic principles were made before the examinations of ox-gall by Strecker, in 1848. The bile is, however, one of the most important, but least understood, of the animal fluids; and our scanty information with regard to its functions has been in a measure due to the want of an exact knowledge of its physiological chemistry. We shall study the composition of the bile very closely, and shall show that it contains two classes of constituents; one class—elements of secretion—which is reabsorbed; and another—an element of excretion—which is discharged in a modified form in the fæces. The latter involves a newly-described function of the liver, but our information is much more positive and definite concerning it than with regard to the digestive action of the bile. In treating of the subject of digestion, we have already indicated some of the difficulties, which have been but imperfectly overcome, in the study of the action of the bile as a true secretion, or a recrementitious fluid. The reason why the same obscurity has prevailed, until very recently, with regard to the function of the bile as an excretion is that physiologists have regarded what are known as the biliary salts as the only really important constituents; and these salts have eluded chemical investigation after the discharge of the bile into the small intestine. Our recent posi-

tive knowledge of the excrementitious function of the liver is due to the recognition of cholesterine, an invariable constituent of the bile, as one of the most important of the elements of excretion.

Composition of Human Bile.[1]

Water	915·00 to 819·00
Taurocholate, or choleate of soda ($NaO,C_{52}H_{45}NO_{14}S_2$)	56·50 " 106·00
Glycocholate, or cholate of soda ($NaO,C_{52}H_{42}NO_{11}$)	traces.
Cholesterine ($C_{26}H_{22}O$)	1·60 to 2·66
Biliverdine	14·00 " 30·00
Lecithene } Margarine, oleine, and traces of soaps. }	3·20 " 31·00
Choline ($C_{10}H_{13}NO_2$)	traces.
Chloride of sodium	2·77 to 3·50
Phosphate of soda	1·60 " 2·50
Phosphate of potassa	0·75 " 1·50
Phosphate of lime	0·50 " 1·35
Phosphate of magnesia	0·45 " 0·80
Salts of iron	0·15 " 0·30
Salts of manganese	traces " 0·12
Silicic acid	0·03 " 0·06
Mucosine	traces.
Loss	3·45 to 1·21
	1,000·00 1,000·00

There are no peculiarities in the composition of the bile, as regards its inorganic constituents, which demand more than a passing mention. It contains no coagulable organic principle, except mucosine, and all of its constituents are simply solids in solution. The quantity of solid matter is very large, and the proportion of water relatively small; but in comparing its proportion of water with that of other fluids in the body, as the blood-plasma, lymph and chyle, milk, etc., it must be remembered, as is suggested by

[1] This table of the composition of the bile is compiled from Robin (*Leçons sur les humeurs*, Paris, 1867, p. 542). In making up the table, the difference between the sum of the constituents and 1,000 has been put in as "loss." We have omitted leucine, tyrosine, and urea, as their existence as proximate principles of normal bile is doubtful.

Robin,[1] that all of these contain water entering into the composition of their coagulable principles; so that their proportion of water, as it is ordinarily given, is really not greater than in the bile. Among the inorganic salts, we find chloride of sodium in considerable quantity, and a large proportion of phosphates. We also note the presence of salts of iron, of manganese, and a small proportion of silicic acid.[2]

The fatty and saponaceous matters demand hardly any more extended consideration. A small quantity of margarine and oleine are held in solution, partly by the small proportion of soaps, but chiefly by the taurocholate of soda. These principles sometimes exist in larger quantity, and may be discovered in the form of globules. The proportion of soaps is very small. Lecithene, a phosphorized fat, is mentioned by Robin and others, but its constitution is not definitely settled. All that is known of this principle is that it is a neutral fatty substance extracted from the bile, and is capable of being decomposed into phosphoric acid and glycerine. Choline ($C_{10}H_{13}NO_2$) is a peculiar alkaloid found in the bile in exceedingly minute quantity.

Biliary Salts.

The principles which we have called biliary salts are compounds of soda with peculiar organic acids, found nowhere but in the liver, and undoubtedly produced in this organ from materials furnished by the blood. The fact that the bile possesses peculiar principles has long been recognized. It is unnecessary, however, to follow out in detail the earlier chemical investigations into their properties; for the biliary matter of Berzelius and the picromel and biliary resin of Thenard are now known to be composed of several distinct proximate principles. Our exact knowledge

[1] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 543.

[2] The presence of hydrochlorate of ammonia and the ammonio-magnesian phosphate has lately been indicated in the bile by M. Bergeret (de Saint-Léger) —*Journal de l'anatomie*, Paris, 1869, tome vi., p. 437.

of these substances dates from the analysis of ox-bile by Strecker. He obtained two peculiar acids, cholic and choleic acid, which he found in the bile, in combination with soda.[1] In the subsequent researches of Lehmann, these acids are called, respectively, glycocholic and taurocholic acid, and the salts, glycocholate and taurocholate of soda.[2]

In human bile, the proportion of glycocholate of soda is very small, the biliary matter existing almost entirely in the form of the taurocholate. The taurocholate may be precipitated from an alcoholic extract of bile by ether, in the form of dark, resinous drops. These do not crystallize, and the amount of glycocholate, which is precipitated in the same way and soon assumes a crystalline form, is very slight. Prof. Dalton, who has studied the biliary salts very closely, at first was unable to obtain any crystalline matter from human bile, but he has lately found it in minute quantity.[3]

Taurocholate of Soda ($NaO,C_{52}H_{44}NO_{13}S_2$).—There is some doubt whether the resinous drops obtained by the addition of an excess of ether to a strong alcoholic extract of bile consist of a proximate principle in a perfectly pure state. These drops are not crystallizable, and this has led to the opinion, expressed by Robin and Verdeil, that they are impure.[4] In fact, even now, there is a certain amount of obscurity with regard to the character of these peculiar biliary salts. In ox-bile, the non-crystallizable and the crystallizable salts exist together; but in human bile, the

[1] STRECKER, *Untersuchung der Ochsgalle.—Annalen der Chemie und Pharmacie*, Heidelberg, 1848, Bd. lxv., S. 1, *et seq.*; *Beobachtungen über die Galle verschiedener Thiere*, Idem, 1849, Bd. lxx., S. 149, *et seq.* An analysis of these observations is given in the *Journal de pharmacie et de chimie*, Paris, 1848, tome xiii., p. 215; 1849, tome xv., p. 153; and tome xvi., p. 450.

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. ii., p. 201, *et seq.*

[3] DALTON, *Treatise on Human Physiology*, Philadelphia, 1867, p. 167.

[4] ROBIN ET VERDEIL, *Traité de chimie anatomique*, Paris, 1853, tome ii., p. 473.

greatest part is in the form of what we know as the tauro-cholate of soda.

These salts may be readily obtained from ox-bile and separated from each other by the following process: The bile is first evaporated to dryness and pulverized. The dry residue is then extracted with absolute alcohol and filtered. In this part of the process, Dr. Dalton uses five grains of the dry residue to one fluidrachm of alcohol.[1] The filtered fluid is of a clear, yellowish color, and contains fats and coloring matter, in addition to the biliary salts. To precipitate the biliary salts, a small quantity of ether is added, which produces a dense, white precipitate that redissolves by agitation. Another small quantity of ether is again added, and the precipitate thus produced is dissolved by shaking the mixture. This process is repeated carefully, adding the ether and shaking the mixture after each step, until the precipitate becomes permanent. An excess of ether—from eight to ten times the bulk of the alcoholic extract used—is then added, the test-tube or flask is carefully corked, and the mixture is set aside to crystallize. Gradually the dense, white precipitate falls to the bottom of the vessel or becomes attached in the form of resinous drops to the sides of the glass; and in from six to twenty-four hours it begins to form delicate acicular crystals, arranged in rosettes. These are crystals of the glycocholate of soda; and the non-crystallizable matter remaining is the taurocholate of soda.

To separate these two salts, the ether is rapidly poured off, and the crystalline and resinous residue is dissolved in distilled water. On the addition to this solution of a little acetate of lead, the glycocholate is decomposed and precipitated in the form of glycocholate of lead, leaving the tauro-

[1] DALTON, *Treatise on Human Physiology*, Philadelphia, 1867, p. 162, *et seq.*, and *On the Constitution and Physiology of the Bile.—American Journal of the Medical Sciences*, Philadelphia, 1857, New Series, vol. xxxiv., p. 305, *et seq.* The details of the processes for the extraction of the biliary salts are taken from Dalton, who has studied this subject very carefully, and whose method is simple and entirely satisfactory.

cholate in solution. The glycocholate of lead is then separated by filtration, and the subacetate of lead is added to the filtered fluid. This decomposes the taurocholate, and the taurocholate of lead is precipitated. The subacetate of lead will decompose both the glycocholate and the taurocholate, but the glycocholate only is acted upon by the acetate of lead. The glycocholate and the taurocholate of lead are then carefully washed and treated separately with the carbonate of soda, which gives the original salts in nearly a pure state.

The taurocholate of soda is a proximate principle of the bile, and it is not necessary to describe fully in detail the purely chemical processes by which it is decomposed. With a little care, the taurochôlic acid may be obtained in a state of tolerable purity, and by prolonged boiling with potash, may be decomposed into a new acid and taurine. Some confusion exists in the books about the name of this new acid. Strecker calls it cholalic acid, and applies the name of cholic acid to what we have described as glycocholic acid. As we have adopted the nomenclature of Lehmann, we shall call it cholic acid. Its formula is $C_{48}H_{39}O_9HO$. The formula for taurine is $C_4H_7NO_6S_2$. It must be remembered, however, that these substances are formed artificially and are not true proximate principles. They have been described in explanation of the name taurocholic acid, which has been applied to it on the assumption that the different biliary acids are formed of cholic acid united with taurine or other basic substances.

If human bile be treated in the manner just described, frequently no crystalline matter is obtained, and when it exists, it is in very small quantity. The great mass of the precipitate is composed of the taurocholate of soda. This, when it has been thoroughly purified, is whitish and gummy, very soluble in water and alcohol, and insoluble in ether. It is melted with slight heat, and is inflammable. Its reaction is neutral. It has a peculiar, sweetish-bitter taste. The

tion of this principle in the bile is always very large, subject to considerable variation. It has very little mmon with the salts of fatty origin, either in its general rties or composition, inasmuch as it is entirely insolu- n ether, and its acid contains nitrogen. Another pecu- ty in its composition, and one which serves to distinguish rom the glycocholate of soda, is that it contains two ms of sulphur. One of its important properties in the e is that it aids in the solution of the fats contained in is fluid, and to a certain extent, probably, in the solution f cholesterine.

Glycocholate of Soda ($NaO,C_{52}H_{42}NO_{11}$).—We have ne- cessarily described the process for the extraction of the glycocholate of soda, in connection with the taurocholate. The glycocholate is crystallizable and is more easily obtained in a condition of purity. The chief chemical points of dif- ference between these salts are, that the glycocholate is pre- cipitated by the acetate of lead as well as the subacetate, the acetate having no effect upon the taurocholate of soda, and that the glycocholic acid does not contain sulphur. By treating glycocholic acid with potash at a high temperature, it is decomposed into cholic acid and glycine, or glycocoll ($C_4H_5NO_4$). It is this which has given it the name of glyco- cholic acid. In their physiological relations, the two biliary salts are, as far as we know, identical.

Origin of the Biliary Salts.—There can be no doubt that these principles are elements of secretion, and are pro- duced *de novo* in the substance of the liver. In no instance have they ever been discovered in the blood in health; and, although they present certain points of resemblance with some of the constituents of the urine, they have never been found in the excreta. In experiments made by Müller,[1]

[1] MUELLER, *Manual de physiologie*, Paris, 1851, tome i., p. 122.

Kunde,[1] Lehmann,[2] and Moleschott,[3] on frogs, in which the liver was removed and the animal survived several days, and in the observations of Moleschott, between two and three weeks, it was found impossible to determine the accumulation of the biliary salts in the blood. There is no reason, therefore, for supposing that these principles are products of disassimilation. Once discharged into the intestine, they undergo certain changes, and can no longer be recognized by the usual tests; but experiments have shown that, changed or unchanged, they are absorbed with the elements of food.[4] They are probably the elements concerned in the digestive function of the bile.

Cholesterine, $C_{26}H_{22}O$.

Before the publication, in 1862, of a memoir on a new excretory function of the liver, the function and relations of cholesterine were not known, and this substance was hardly mentioned in most works on physiology. As we believe that it must now be recognized as one of the most important of the products of disassimilation, it becomes interesting and important to study its properties more closely.

The first description we have of cholesterine is by Fourcroy, who states that it was discovered by Poulletier de la Salle, in 1782.[5] Fourcroy also described adipocire, which he likened to cholesterine, although he did not con-

[1] KUNDE, *De Hepatis Extirpatione, Dissertatio Inauguralis*, Berolini, 1850.

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 476.

[3] MOLESCHOTT, *Sur la sécrétion du sucre et de la bile dans le foie.—Comptes rendus*, Paris, 1855, tome xl., p. 1040.

Moleschott was more successful, in these experiments, than any of those who had preceded him. He extirpated the liver from a great number of frogs, and succeeded in keeping them alive for two or three weeks; but he could never detect in the blood the bile-pigment or the biliary salts.

[4] See vol. ii., Digestion, p. 374, *et seq.*

[5] FOURCROY, *Mémoire sur la nature des altérations qu'éprouvent quelques humeurs animales, par l'effet des maladies et par l'action des remèdes.—Mémoires de la Société Royale de Médecine*, 1782–1783, Paris, 1788, p. 489. The substance

sider the two substances identical.[1] In 1814, Chevreul gave a full description of cholesterine, and extracted it from the bile of the human subject and some of the inferior animals.[2] It was afterward found by different observers, in gall-stones, intestinal concretions, cysts, and tumors. In 1830, Denis described a substance in the blood, which he thought was cholesterine, and its discovery in this fluid is attributed to him by most authors; but in 1838, he acknowledged the error of his first observation,[3] and admits that cholesterine, with a new substance analogous to it, called seroline, was discovered in the blood, in 1833, by Boudet.[4]

Cholesterine is now recognized as a normal constituent of various of the tissues and fluids of the body. Most authors state that it is found in the bile, blood, liver, nervous tissue, crystalline lens, meconium, and fæcal matter. We have found it in all these situations, with the exception of the fæces,[5] where it does not exist normally, having been transformed into stercorine in its passage down the intestinal canal.[6]

In the fluids of the body, cholesterine exists in solution; but by virtue of what constituents it is held in this condition,

described by Fourcroy was undoubtedly cholesterine; but it remained for Chevreul to describe its properties accurately and give it the name by which it is now known. The observations of Chevreul will be referred to farther on.

[1] FOURCROY, *Deuxième mémoire sur les matières animales trouvées dans la Cimetière des Innocens à Paris.—Annales de chimie*, Paris 1791, tome viii., p. 62, *et seq.*

[2] CHEVREUL, *Recherches chimiques sur plusieurs corps gras, Cinquième mémoire. Des corps qu'on a appellé adipocire.—Annales de chimie*, Paris, 1815, tome xcvi., p. 7.

[3] DENIS, *Essai sur l'application de la chimie à l'étude physiologique du sang de l'homme*, Paris, 1838, p. 147.

[4] BOUDET, *Nouvelles recherches sur la composition du sérum du sang humain.—Annales de chimie et de physique*, Paris, 1833, tome lii., p. 337.

[5] For a table of the quantities of cholesterine in various situations, see an article by the author, on a *New Excretory Function of the Liver.—American Journal of the Medical Sciences*, Philadelphia, 1862, New Series, vol. xliv., p. 313.

[6] See vol. ii., Digestion, p. 399, *et seq.*

is not entirely settled. It is stated that the biliary salts have the power of holding it in solution in the bile, and that the small amount of fatty acids contained in the blood hold it in solution in that fluid; but direct experiments on this point are wanting. In the nervous substance and in the crystalline lens, it is united "*molecule à molecule*" to the other elements which go to make up these tissues. After it is discharged into the intestinal canal, when it is not changed into stercorine, it is to be found in a crystalline form; as in the meconium, and in the fæces of animals in a state of hibernation. In pathological fluids and in tumors, it is found in a crystalline form, and may be detected by microscopic examination.

Cholesterine is usually described as a non-nitrogenized principle, having all the properties of the fats, except that of saponification with the alkalies. Its chemical formula is given as $C_{26}H_{22}O$. It is neutral, inodorous, crystallizable, insoluble in water, soluble in ether, very soluble in hot alcohol, though sparingly soluble in cold. It is inflammable, and burns with a bright flame. It is not attacked by the alkalies, even after prolonged boiling. When treated with strong sulphuric acid, it strikes a peculiar red color, which is mentioned by some as characteristic of cholesterine. We have found that it possesses this character in common with the so-called seroline.[1]

Cholesterine may easily and certainly be recognized by the form of its crystals, the characters of which can be made out by means of the microscope. They are rectangular or rhomboidal, exceedingly thin and transparent, of variable size, with distinct and generally regular borders, and frequently arranged in layers, with the borders of the lower strata showing through those which are superimposed. This arrangement of the crystals takes place when cholesterine is present in considerable quantity. In pathological speci-

[1] This similarity in the reactions of cholesterine and seroline with sulphuric acid is mentioned by Bérard (*Cours de physiologie*, Paris, 1851, tome iii., p. 117).

mens, the crystals are generally few in number and isolated. The plates of cholesterine are frequently marked by a cleavage at one corner, the lines running parallel to the borders; and frequently they are broken, and the line of fracture is generally undulating. Lehmann attaches a great deal of importance to measurements of the angles of the rhomboid. According to this author, the obtuse angles are 100° 30′, and the acute 79° 30′.[1] We have examined a great number of specimens of cholesterine, extracted from the blood, bile, brain, liver, and occurring in tumors, and have not observed that the crystals have definite angles. Frequently the plates are rectangular, and sometimes almost lozenge-shaped. It is by the transparency of the plates, the parallelism of their borders, and their tendency to break in parallel lines, that we recognize cholesterine. Lehmann seems to consider the tablets of this substance as regular crystals having invariable angles. From examination during crystallization, it seems more probable that they are not crystals, but fragments of micaceous sheets, which, from their extreme tenuity, are easily broken. In examining a specimen from the meconium, which was simply extracted with hot alcohol, it was easy to observe a transparent film forming on the surface of the alcohol soon after it cooled, and this, on microscopic examination, *in situ*, disturbing the fluid as little as possible, was found to be marked by long parallel lines. When the fluid had partially evaporated, the crust became broken and the fragments took the form of the ordinary crystals of cholesterine, but they were larger and more regular. The tablets were exceedingly thin, and regularly divided into delicate plates, with the characteristic corner-cleavages of the cholesterine; and as the focus of the instrument was changed, new layers were brought into view.

Crystals of cholesterine melt at 293° Fahr., but are formed again when the temperature falls below that point. According to Lehmann, they may be distilled *in vacuo* at 680°,

[1] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 244.

without decomposition. The determination of the fusing point is one of the means of distinguishing it from seroline,[1] which fuses at 90° 8′.

Without considering in detail the processes which have been employed by other observers for the extraction of cholesterine from the blood, bile, and various tissues of the body, we shall simply describe the method which has been found most convenient in the various analyses we have made for this substance. In analyses of gall-stones, the process is very simple; all that is necessary being to pulverize the mass, extract it with boiling alcohol, and filter the solution while hot, the cholesterine being deposited on cooling. If the crystals be colored, they may be redissolved, and filtered through animal charcoal. This is the process employed by Poulletier de la Salle, Fourcroy, and Chevreul. It is only when this substance is mixed with fatty matters, that its isolation is a matter of any difficulty. In extracting cholesterine from the blood, we have operated on both the serum and clot, and in this way have been able to demonstrate it in greater quantities in this fluid than have been observed by others, who have employed only the serum. The following is the process for quantitative analysis, which was determined upon after a number of experiments:

The blood, bile, or brain, as the case may be, is first carefully weighed, then evaporated to dryness over a water-bath, and pulverized in an agate mortar. The powder is then treated with ether, in the proportion of about a fluidounce for every hundred grains of the original weight, for from twelve to twenty-four hours, agitating the mixture occasionally. The ether is then separated by filtration, throwing a little fresh ether on the filter so as to wash through every trace of the fat, and the solution set aside to evaporate. If the fluid, especially the blood, have been carefully dried and pulverized, when the ether is added, it divides it into a very fine powder and penetrates every part. After the ether has

[1] Lehmann, *loc. cit.*

evaporated, the residue is extracted with boiling alcohol, in the proportion of about a fluidrachm for every hundred grains of the original weight of the specimen, filtered while hot into a watch-glass, and allowed to evaporate spontaneously. To keep the fluid hot while filtering, the whole apparatus may be placed in the chamber of a large water-bath, or, as the filtration is generally rapid, the funnel may be warmed by plunging it into hot water, or steaming it, taking care that it be carefully wiped. We now have the cholesterine mixed with a certain quantity of saponifiable fat. After the fluid has evaporated, we can see the cholesterine crystallized in the watch-glass, mingled with masses of fat. This we remove by saponification with an alkali; and for this purpose, we add a moderately strong solution of caustic potash, which we allow to remain in contact with the residue for from one to two hours. If much fat be present, it is best to heat the mixture to a temperature a little below the boiling point; but in analyses of the blood this is not necessary. The mixture is then to be largely diluted with distilled water, thrown upon a small filter, and thoroughly washed till the fluid which passes through is neutral. We then dry the filter, and fill it up with ether, which, in passing through, dissolves out the cholesterine. The ether is then evaporated, the residue extracted with boiling alcohol, as before, the alcohol collected on a watch-glass previously weighed, and allowed to evaporate. The residue consists of pure cholesterine, the quantity of which may be estimated by weight.

The accuracy of this process may be tested by means of the microscope; for the crystals have so distinctive a form, that it is easy to determine, by examining the watch-glass, whether the cholesterine be perfectly pure. In making this analysis quantitatively, it is necessary to be very careful in all the manipulations; and for determining the weight of such minute quantities, an accurate and delicate balance, one, at least, that will turn with the thousandth of a gramme, carefully adjusted, must be employed. With these precau-

tions, the quantity of cholesterine in any fluid or solid may be determined with perfect accuracy; and the estimate may be made in so small a quantity as from fifteen to twenty grains of blood. In analyzing the brain and bile, we found it necessary to pass the first ethereal solution through animal charcoal, to get rid of the coloring matter. In doing this, the charcoal must be washed with fresh ether till the solution which passes through is brought up to the original quantity. The other manipulations are the same as in examinations of the blood. In examining the meconium, we found that the cholesterine which crystallized from the first alcoholic extract was so pure that it was not necessary to subject it to the action of an alkali.

The proportion of cholesterine in the bile is not very large. In the table, it is estimated at from 1·60 to 2·66 parts per thousand. In a single examination of the human bile, we found the proportion 0·618 of a part per thousand.

The origin and destination of this principle involve, as we believe, an office of the liver which has not hitherto been recognized by physiologists; and we shall consider these questions specially, under the head of the excretory function of the liver.

Biliverdine.

The coloring matter of the bile bears a certain resemblance to the coloring matter of the blood, and is supposed to be formed from it in the liver. It gives to the bile its peculiar tint, and has, as we have remarked, the property of coloring the tissues with which it comes in contact. Whenever the flow of bile is seriously obstructed, the coloring matter is absorbed by the blood, and can be readily detected in the serum, in the urine, and in the color of the skin and conjunctiva. In the bile it is liquid, but it may be coagulated and extracted by various processes. It does not exist naturally in the form of pigmentary granulations.

This principle is precipitated from the bile by boiling with milk of lime. The filtered residue is then decomposed with hydrochloric acid, which unites with the lime and leaves a fatty residue of an intense-green color. The fat is then removed by repeated washings with ether (a very long and difficult process). The precipitate is then redissolved in alcohol with ether added, which gives to the liquid a bluish-green color, and leaves, after evaporation, a dark-green powder. This powder contains iron, but its proportion has never been accurately estimated. The matter thus obtained is insoluble in water and in chloroform, but is soluble in ether, alcohol, sulphuric and hydrochloric acid.[1]

It is unnecessary to follow out in detail all of the chemical investigations which have been made into the ultimate composition and the modifications of this and the other coloring matters. According to Robin,[2] the empirical formula for biliverdine, deduced from the analyses of Scherer, is $C_{32}H_{18}NO_4$. No account is taken in these analyses of the iron, the existence of which cannot be doubted.

Upon the addition of nitric acid, or better, of nitric mixed with nitrous acid, biliverdine is acted upon in a peculiar way, producing a play of colors, which is recognized as one of the tests for bile.

Tests for Bile.

It is frequently desired, particularly in pathological investigations, to ascertain, by some easy test, the fact of the presence or absence of bile in various of the fluids and solids of the body. It is, indeed, a most interesting physiological question to determine the course and destination of the biliary salts after the bile has passed into the intestinal canal; and this can be done only by the application of appropriate tests to the contents of the alimentary tract and

[1] ROBIN ET VERDEIL, *Traité de chimie anatomique*, Paris, 1853, tome iii., p. 389.

[2] ROBIN, *Leçons sur les humeurs*, Paris, 1867, p. 550.

the blood of the portal system. The ingredients of the bile which it is important to detect are biliverdine, the biliary salts, and cholesterine. The last-named substance can be detected best by applying the method which we have just described for its extraction; but several tests have been proposed for the detection, on the one hand, of the coloring matter of the bile, and on the other, of the peculiar biliary salts.

Test for Biliverdine.—There is one test so simple and easy of application, that it alone will suffice for the prompt detection of biliverdine. This is peculiarly applicable to the urine, where the presence or absence of bile frequently becomes an important question.

We are led generally to suspect the presence of bile in the fluids of the body by the peculiar color. If we spread out the suspected fluid in a thin stratum upon a white surface, as a porcelain plate, and add a single drop of nitric acid, or, what is better, nitroso-nitric acid, if the coloring matter of bile be present, a peculiar play of colors will be observed at the circumference of the drop of acid as it diffuses itself. The color will rapidly change from blue to red, orange, purple, and finally yellow. This is due to the action of the acid upon the biliverdine; and this test will not indicate the presence of either cholesterine or the biliary salts. It is used, therefore, only when we wish to determine the presence of the coloring matter of the bile.

Test for the Biliary Salts.—The best, and, indeed, the only reliable test for the biliary salts, was proposed many years ago by Pettenkofer,[1] and is now generally known as Pettenkofer's test. This requires some care and practice in its application, but it is entirely reliable; and although it has been objected that there are other substances than the

[1] PETTENKOFER, *Notiz über eine neue Reaction auf Galle und Zucker.—Annalen der Chemie und Pharmacie*, Heidelberg, 1844, Bd. lii., S. 90.

biliary salts which produce similar reactions, these are not met with in the animal fluids, and consequently are not liable to produce confusion. If a considerable quantity of bile be present in any fluid, and if there be not a large admixture of animal matters, the test may be employed without any preparation; but in delicate examinations, it is best to evaporate the suspected liquid, extract the residue with absolute alcohol, precipitate with ether, and dissolve the ether-precipitate in distilled water. By this means a clear solution is obtained, which will react distinctly, even when the biliary salts exist in very small quantity. Pettenkofer's test is applicable to any of the biliary salts, whatever be their form, and the reaction is dependent upon the presence of cholic acid, which enters into the composition of all the varieties of the biliary acids.

The following is one of the most common methods of employing Pettenkofer's test: To the suspected solution we add a few drops of a strong solution of cane-sugar in water. Sulphuric acid is then slowly added, to the extent of about two-thirds of the bulk of the liquid. It is recommended to add the acid slowly, so that the temperature shall be but little raised. If a large quantity of the biliary salts be present, a red color shows itself almost immediately at the bottom of the test-tube, and soon extends through the entire liquid, rapidly deepening until it becomes of a dark-lake or purple. If the biliary matters exist in very small proportion, it may be several minutes before any red color makes its appearance, and the change to a purple is correspondingly slow, the whole process occupying from fifteen to twenty minutes. Many organic matters may be rendered dark by the action of the acid, and the sugar itself will be acted upon, even if no bile be present, but the color due to the sugar alone is yellow. The peculiar play of colors above described can easily be recognized after a little practice, and is observed only in the presence of the biliary salts.

The ordinary modifications in the application of this test

are unimportant. Some recommend to add the sulphuric acid first, and then to add the solution of sugar; and some, after adding to the liquid two-thirds of its volume of sulphuric acid, drop into the mixture one or two lumps of cane-sugar. The reaction with the biliary salts is essentially the same, whichever of these methods be employed.

Excretory Function of the Liver.

In 1862, in studying the properties and physiological relations of cholesterine, we gave the first definite account of an excretory function of the liver. The experiments and observations upon which we based our conclusions were extended and laborious, and, as far as we know, have not been repeated in detail by other observers; but the results must be taken as positive, if the accuracy of the experiments be admitted, and they have been adopted, to a greater or less extent, by scientific authorities. The details of these experiments are too elaborate to be given in full, as contained in the original memoir.[1]

The few statements with regard to the function of cholesterine to be found in works published before 1862 are very indefinite. In most works on physiology, this substance is hardly mentioned, it being generally regarded as a curious principle, interesting only to the physiological chemist. We have given, in the memoir referred to, extracts from the works of Carpenter, Lehmann, Mialhe, and Dalton, which contain all that is said of the probable function of cholesterine; and these quotations, which embody about all that we could find on the subject, show that its office was not in the least understood. Inasmuch as cholesterine is the only excrementitious principle as yet discovered in the bile, bearing the same relation to this fluid that urea does to the urine,

[1] FLINT, JR., *Experimental Researches into a New Excretory Function of the Liver.—American Journal of the Medical Sciences*, Philadelphia, 1862, New Series, vol. xliv., p. 305, *et seq.*; and *Recherches expérimentales sur une nouvelle fonction du foie*, Paris, 1868. (See note on page 294.)

it is evident that the ideas of physiologists, with regard any excretory function of the liver, must have been v indefinite before the relations of cholesterine had been termined.

The first question which arises is whether the liver h any excretory function. Some authors, notably Blondlot have assumed that the bile is purely excrementitious and has no function as a secretion. This question we have fully discussed in another place.[1] The confusion that has arisen with regard to this point has been due to the fact that those who adopted the view that the bile was simply an excretion denied to it any digestive properties; while, on the other hand, those who believed it to be concerned in digestion would not admit that it was an excretion. We have shown conclusively, in treating of intestinal digestion, that the bile is so important in this process as to be essential to life; bu we have shown, at the same time, that the liver eliminate from the blood one of the most important of the products o disassimilation. It will be found important, as bearing upon the probable function of the bile, to apply to this fluid th general considerations contained in our first chapter, on th distinctions between secretions and excretions.

Cells of glandular epithelium are constantly manufac turing, out of materials furnished by the blood, the element of the true secretions; but these elements do not preëxi in the blood, they appear *de novo* in the secreting orga and never accumulate in the system when the function of th secreting organ is disturbed. Again, the true secretions a not discharged from the body, but have a function to perfor in the economy, and are poured out by the glands intermi tently, at the times when this function is called into actio As far as the biliary salts (the taurocholate and glycocholat of soda) are concerned, the bile corresponds entirely to th true secretions. These principles are manufactured by th liver, they do not preëxist in the blood, and they do not a

[1] See vol. ii., Digestion, p. 362, *et seq.*

cumulate in the blood when their formation in the liver is disturbed. The researches of Bidder and Schmidt and others have shown that although we cannot detect the biliary salts in the blood or chyle coming from the intestine, these principles are not discharged in the fæces.[1] All of these facts point to an important function of the bile as a secretion. It is true that it is discharged constantly, but during digestion its flow is very much more abundant than at any other time. It is pretty well established that during the intervals of the flow of the secretions, the glands are manufacturing the materials of secretion, which are washed out, as it were, in the great afflux of blood which takes place during what has been called the functional activity of the gland. Now if the liver, in addition to its function as a secreting organ, be constantly forming bile for the purpose of eliminating an excrementitious matter, it is to be expected that the bile would always contain a certain proportion of its elements of secretion.

The constant and invariable presence of cholesterine in the bile assimilates it in every regard to the excretions, of which the urine may be taken as the type. Cholesterine always exists in the blood and in certain of the tissues of the body. It is not produced in the substance of the liver, but is merely separated from the blood by this organ. It is constantly passed into the intestine, and is discharged, although in a modified form, in the fæces. We know of no function which it has to perform in the economy, any more than urea, or any other of the excrementitious principles of the urine; and we have shown, in the memoir already referred to, that it accumulates in the blood in certain cases of organic disease of the liver and gives rise to certain symptoms of blood-poisoning.

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bile contained in this organ—the crystalline lens, and the spleen;[1] but with these exceptions, it is found only in the nervous system and blood. Two views present themselves with regard to its origin. It is either deposited in the nervous matter from the blood, or is formed in the brain and taken up by the blood. This is a question, however, which can be settled experimentally, by analyzing the blood for cholesterine as it goes to to the brain by the carotid, and as it comes from the brain by the internal jugular. The cholesterine being found also in the nerves, and, of course, a large quantity of nervous matter existing in the extremities, it is desirable at the same time to make an analysis of the venous blood from the general system.

With a view of determining this question, we made the following experiments:

Experiment I.—In this experiment, specimens of blood were taken from the carotid, the internal jugular, the vena cava, hepatic veins, hepatic artery, and portal vein, in a living animal (a dog about six months old). In addition, we took a specimen of bile from the gall-bladder, and some of the substance of the brain. These were all carefully examined for cholesterine, and the following were the main results: In the brain cholesterine was found in large quantity. There was no cholesterine in the extract of the blood from the carotid, examined three days after, and but a few crystals, eleven days after. Cholesterine was almost immediately discovered in the extract of the blood from the internal jugular, and the crystals were present in large numbers on the twelfth day. In this experiment the animal was etherized when the blood was taken, and the examinations

[1] In 1854, Marcet described a substance extracted from the spleen, which he thought was analogous to cholesterine (*An account of the Organic Chemical Constituents, or Immediate Principles of the Excrements of Man and Animals in the Healthy State.—Philosophical Transactions*, London, 1854, p. 269); and in 1857, he fully recognized its existence in this organ (*On the Immediate Principles of the Excrements of Man and Animals in the Healthy State.—Philosophical Transactions*, London, 1857, p. 412).

for cholesterine were not quantitative. In the succeeding experiments, the proportion of cholesterine in the different specimens of blood was accurately estimated, and, in most of them, no anæsthetic was used during the operative procedure.

Experiment II.—A medium-sized adult dog was put under the influence of ether, and the carotid artery, internal jugular, and femoral vein exposed. Specimens of blood were drawn, first from the internal jugular, next from the carotid, and last from the femoral vein. These specimens were received into carefully-weighed vessels, and weighed.

They were then analyzed for cholesterine by the process already described, and the following results obtained:

	Quantity of Blood. *grains.*	Cholesterine. *grains.*	Cholesterine per 1,000 pts.
Carotid	179·462	0·139	0·774
Internal jugular	134·780	0·108	0·801
Femoral vein	133·886	0·108	0·806

Percentage of increase in the blood from the jugular over the arterial blood .... 3·488

Percentage of increase in the blood from the femoral vein .... 4·134

This experiment shows an increase in the quantity of cholesterine in the blood in its passage through the brain, and an increase, even a little greater, in the blood passing through the vessels of the posterior extremity. To facilitate the operation, however, the animal was brought completely under the influence of ether, which, from its action on the brain, would not improbably produce some temporary disturbance in the nutrition of that organ, and consequently interfere with the experiment. For the purpose of avoiding this difficulty, we performed the following experiments without administering an anæsthetic:

Experiment III.—A small young dog was secured to the operating-table, and the internal jugular and carotid exposed on the right side. Blood was taken, first from the jugular, and afterward from the carotid. The femoral vein

on the same side was then exposed, and a specimen of blood was taken from that vessel. The animal was very quiet under the operation, though no anæsthetic was used, so that the blood was drawn without any difficulty and without the slightest admixture.

The three specimens were analyzed for cholesterine, with the following results:

	Quantity of Blood. *grains.*	Cholesterine. *grains.*	Cholesterine per 1,000 pts.
Carotid	143·625	0·679	0·967
Internal jugular	29·956	0·046	1·545
Femoral vein	45·035	0·046	1·028

Percentage of increase in the blood from the jugular over the arterial blood .... 59·772
Percentage of increase in the blood from the femoral vein .... 6·308

Experiment IV.—A large and powerful dog was secured to the operating-table, and the carotid and internal jugular exposed. Specimens of blood were taken from these vessels, first from the jugular, and were carefully weighed and analyzed for cholesterine in the usual way. The following results were obtained:

	Blood. *grains.*	Cholesterine. *grains.*	Cholesterine per 1,000 pts.
Carotid	140·847	0·108	0·768
Internal jugular	97·811	0·092	0·947

Percentage of increase in the blood passing through the brain .... 23·307

Experiment III. shows a very considerable increase in the quantity of cholesterine in the blood passing through the brain, while the increase is comparatively slight in the blood of the femoral vein. The proportion of cholesterine is also large in the arterial blood, compared with other observations.

Experiment IV. shows but a slight difference in the quantity of cholesterine in the arterial blood in the two animals; the proportion in the animal that was etherized being 0·774 per 1,000, and in the animal that was not etherized 0·768 per 1,000, the difference being but 0·006; but, as was suspected, the ether seemed to have an influence on the quan-

tity of cholesterine absorbed by the blood in its passage through the brain. In the first instance the increase was but 3·488 per cent., while in the latter it was 23·307 per cent.

The natural conclusions to be drawn from these observations, with regard to the origin of cholesterine in the economy, are the following: It has been ascertained that the brain and nerves contain a large quantity of this substance, which is found in hardly any other of the tissues of the body; and these experiments, especially Experiments III. and IV., show that the blood that comes from the brain contains a much larger quantity of cholesterine than the blood supplied to this organ.

The conclusion is, then, that cholesterine is produced in the brain, and is taken up by the blood as it passes through this organ.

But the brain is not the only part where cholesterine is produced. It will be seen by Experiment II. that there is 4·134 per cent., and in Experiment III. 6·308 per cent. of increase in the cholesterine in the passage of the blood through the inferior extremities, and probably about the same in other parts of the muscular system. In examining these tissues chemically, we find that the muscles contain no cholesterine, but that it is abundant in the nerves; and as we have found that the proportion of cholesterine is immensely increased in the passage of the blood through the great centre of the nervous system, taken, as the specimens were, from the internal jugular, which collects the blood mainly from the brain and very little from the muscular system, it is rendered very probable that, in the general venous system, the cholesterine which the blood contains is produced in the substance of the nerves.

If this be true, and if cholesterine be one of the products of the disassimilation of nervous tissue, its formation would be proportionate in activity to the nutrition of the nerves; and any thing which interfered to any great extent with their nutrition would diminish the quantity of choleste-

rine produced. In the production of urea by the general system, which is an analogous process, muscular activity increases the quantity, and inaction diminishes it, on account of the effect upon nutrition. In cases of paralysis, we have a diminution of the nutritive forces in the parts affected, especially of the nervous system, which, after a time, becomes so disorganized that although the cause of the paralysis be removed, the nerves cannot resume their functions. It is true we have this disorganization taking place to a certain extent in the muscles, but it is by no means as marked as it is in the nerves. We should be able, then, to confirm the observations on animals, by examining the blood in cases of paralysis, when we should expect to find a very marked difference in the quantity of cholesterine, between the venous blood coming from the paralyzed parts, and the blood from other parts of the body. With this point in view we made analyses of the blood from both arms, in three cases of hemiplegia.

Case I.—Sarah Rumsby, æt. 47, was affected with hemiplegia of the left side. Two years ago she was taken with apoplexy, and was insensible for three days. When she recovered consciousness, she found herself paralyzed on the left side. She said she had epilepsy four or five years before the attack of apoplexy. Now she has entire paralysis of motion on the affected side, with the exception of some slight power over the fingers, but sensation is perfect. The speech is not affected. The general health is good.

Case II.—Anna Wilson, æt. 23, Irish, was affected with hemiplegia of the right side. Four months ago she was taken with apoplexy, from which she recovered in one day, with loss of motion and sensation on the right side. She is now improving and can use the right arm slightly. The leg is not so much improved, because she will make no effort to use it.

Case III.—Honora Sullivan, Irish, æt. 40, was affected with hemiplegia of the right side. About six months ago she was taken with apoplexy, and recovered consciousness

the next day, with paralysis. The leg was less affected than the arm, from the first. The cause was supposed by Dr. Flint, the attending physician, to be due to an embolus. Her condition is now about the same, as regards the arm, but the leg has somewhat improved.

These cases all occurred at the Blackwell's Island Hospital. The treatment in all consisted of good diet, frictions, passive motion, and use of the paralyzed members as much as possible.

A small quantity of blood was drawn from both arms in these three cases. It was drawn from the paralyzed side, in each instance, with great difficulty, and but a small quantity could be obtained.

The specimens were all examined for cholesterine, with the following results:

Table of Quantity of Cholesterine in Blood of Paralyzed and Sound Sides, in three cases of Hemiplegia.

		Blood.	Cholesterine.	Cholesterine per 1,000.
		grains.	*grains.*	
Case I.	Paralyzed side.	55·458	—	The watch-glass contained 0·031 of a grain of a granular substance, but the most careful examination failed to show a single crystal of cholesterine.
Do.	Sound side.	128·407	0·062	0·481.
Case II.	Paralyzed side.	18·381	—	Same as Case I.
Do.	Sound side.	66·396	0·062	0·808.
Case III.	Paralyzed side.	21·842	—	Same as Case I.
Do.	Sound side.	52·261	0·031	0·579.

The result of these examinations is very interesting: not a single crystal of cholesterine was found in any of the three specimens of blood from the paralyzed side, while about the normal quantity was found in the blood from the sound side. As the nutrition of other tissues is interfered with in paraly-

sis, it is impossible to say positively, from these observations alone, that the cholesterine is produced in the nervous system only. But the nutrition of the nerves is undoubtedly most affected; and these observations, taken in connection with the preceding experiments on animals, point very strongly to such a conclusion.

Our experiments upon animals were so marked and invariable in their results, even when performed under different conditions, that they can leave hardly any doubt of the fact that the blood, in passing through the brain, takes up cholesterine. It is more difficult to show, by actual demonstration, that the general system of nerves also gives up cholesterine to the blood; but the fact that the venous blood coming from the extremities contains more cholesterine than the arterial blood, taken in connection with the fact that none of the tissues of the extremities contain cholesterine, except the nerves, renders it more than probable that the nerves, as well as the brain, are the seat of the formation of this principle.

The observations upon the cases of paralysis are interesting, taken in connection with the experiments on animals. Such observations should, of course, be much more elaborate and extended to lead, of themselves, to positive results; but they go far to confirm our views with regard to the probable origin of cholesterine in the nervous system.

Elimination of Cholesterine by the Liver.—We attempted to demonstrate experimentally the separation of cholesterine from the blood by the liver, in the same way that we demonstrated its passage into the blood circulating through the brain. In the first series of experiments on this subject, we endeavored to show, on the same animal, the origin of cholesterine in certain parts, and the mechanism of its elimination. In these experiments, which were only approximative, as we had not then succeeded in extracting the cholesterine perfectly pure, we commenced with the

arterial blood, examining it as it went into the brain by the carotid, analyzing the substance of the brain, then analyzing the blood as it came out of the brain by the internal jugular, examining the blood as it went into the liver by the hepatic artery and portal vein, examining the secretion of the liver, then the blood as it came out of the liver by the hepatic vein, examining also the blood of the vena cava in the abdomen. The analyses of the blood from the carotid, internal jugular, and vena cava have already been referred to in treating of the origin of the cholesterine. It will be remembered that there was a large quantity of this substance in the internal jugular, and but a small quantity in the carotid, showing that it was formed in the brain. We now give the conclusion of these observations, which bears upon the separation of the cholesterine from the blood:

Experiment I.—Specimens of blood were taken from the hepatic artery, portal vein, and hepatic vein, and a small quantity of bile from the gall-bladder. These specimens were treated in the manner already indicated; viz. evaporated and pulverized, extracted with ether, the ether evaporated, and the residue extracted with boiling alcohol, this evaporated, a solution of caustic potash added, and the specimen then subjected to a microscopical examination.

Microscopical examination of the extract from the portal vein showed quite a number of crystals of cholesterine. These were observed after the fluid had nearly evaporated.

Microscopical examination of the extract from the hepatic artery, made after the fluid had nearly evaporated, showed a considerable amount of cholesterine; more than was observed in the preceding specimen. There were also observed a few crystals of stercorine.

The first examination of the extract from the hepatic vein, which was made just before the potash was added, showed a number of fatty masses, with some crystals of stercorine. The solution of potash was then added, and two days after, another careful examination was made, discov-

ering nothing but fatty globules and granules. The watch-glass was then set aside and was examined eleven days after, when the fluid had entirely evaporated. At this examination, a few crystals of cholesterine were observed for the first time. There were also a number of crystals of margaric and stearic acid.

All the examinations of the extract from the bile showed cholesterine; and the precipitate consisted, indeed, of this substance in a nearly pure state.

Taking these experiments in connection with the first observations on the carotid and internal jugular, while the one series demonstrates pretty conclusively that cholesterine is formed in the brain, the other shows that it disappears, in a measure, from the blood in its passage through the liver, and is passed into the bile. In other words, it is formed in the nervous tissue, and is prevented from accumulating in the blood by its excretion by the liver. This suggests an interesting series of inquiries; and this fact, fully substantiated, would be as important to the pathologist as to the physiologist. But in order to settle this question, it is necessary to do something more than make an approximative estimate of the quantity of cholesterine removed from the blood by the liver. The quantity thus removed in the passage of the blood through this organ should be estimated, if possible, as closely as the quantity which the blood gains in its passage through the brain. But this estimate is more difficult. The operation for obtaining the specimens of blood, in the first place, is much more serious than that for collecting blood from the carotid and internal jugular. It is very difficult to take the unmixed blood from the hepatic vein; and the exposure of the liver, if prolonged, may interfere with its eliminative function, in the same way that exposure of the kidneys arrests, in a few moments, the flow from the ureters. It is probable, however, that the administration of ether does not interfere with the elimination of cholesterine by the liver, as it does, apparently, with its formation

in the brain. Anæsthetics, we know, have a peculiar and special action on the brain, but do not interfere with the functions of vegetative life, such as secretion or excretion; and, we may suppose, would not interfere with the depurative function of the liver. It is fortunate that this is the case, for the operation of taking blood from the abdominal vessels is immensely increased in difficulty by the struggles of an animal that is not under the influence of an anæsthetic.

With the view of settling the question of the disappearance of a portion of the cholesterine of the blood in its passage through the liver, by an accurate quantitative analysis, we repeated the operation for drawing blood from the vessels which go into, and emerge from the liver. In the first trial the blood was drawn so unsatisfactorily, and the operation was so prolonged, that it was not thought worth while to complete the analysis, and the experiment was abandoned. In the following one we were more successful.

Experiment II.—A good-sized bitch (pregnant) was brought completely under the influence of ether, the abdomen laid freely open, and blood drawn, first from the hepatic vein, and next from the portal vein. The taking of the blood was entirely satisfactory, the operation being done rapidly, and the blood collected without any admixture. A specimen of blood was then taken from the carotid, to represent the blood from the hepatic artery.

The three specimens of blood were then examined in the usual way for cholesterine, with the following results:

	Blood. *grains.*	Cholesterine. *grains.*	Cholesterine per 1,000 pts.
Arterial blood...........	159·537	0·200	1·257
Portal vein.............	168·257	0·170	1·009
Hepatic vein............	79·848	0·077	0·964
Percentage of loss in arterial blood in its passage through the liver....			23·309
Do. do. the blood of the portal vein.............			4·460

This experiment proves positively, what there was good ground for supposing from Experiment I., that cholesterine

is separated from the blood by the liver; and here we may note, in passing, a striking coincidence between the analysis in a previous experiment, in which the blood was studied in its passage through the brain, and the one just mentioned, where the blood was studied in its passage through the liver. The gain of the arterial blood in cholesterine in passing through the brain was 23·307 per cent., and the loss of this substance in passing through the liver is 23·309 per cent. There must be, of course, the same quantity separated by the liver that is produced by the nervous system, it being formed, indeed, only to be separated by this organ, its formation being continuous, and its removal necessarily the same, in order to prevent its accumulation in the circulating fluid. The almost exact coincidence between these two quantities, in specimens taken from different animals, though not at all necessary to prove the fact just mentioned, is still very striking.

It is shown by Experiment II. that the portal blood, as it goes into the liver, contains but a small percentage of cholesterine over the blood of the hepatic vein, while the percentage in the arterial blood is large. The arterial blood is the mixed blood of the entire system; and as it probably passes through no organ before it gets to the liver, that diminishes its cholesterine, it contains a quantity of this substance, which must be removed. The portal blood, coming from a limited part of the system, contains less cholesterine, though it gives up a certain quantity. In the circulation of the liver, the portal system largely predominates, and is necessary to other important functions of this organ, such as the production of sugar; but soon after the portal vein enters the liver, its blood becomes mixed with that from the hepatic artery, and from this mixture the cholesterine is separated. It is only necessary that blood, containing a certain quantity of cholesterine, should come in contact with the bile-secreting cells, in order that this substance be separated. The fact that it is eliminated by the liver is proven

with much less difficulty than that it is formed in the nervous system. In fact, its presence in the bile, and the necessity of its constant removal from the blood, consequent on its constant formation and absorption by this fluid, are almost sufficient in themselves to warrant the conclusion that it is removed by the liver. This, however, is put beyond a doubt by the preceding analyses of the blood going to and coming from this organ.

In treating of the composition of the fæces, we have considered so fully the changes which the cholesterine of the bile undergoes in its passage down the intestinal canal, that it is not necessary to refer to this portion of the subject again.[1] We have made but one examination of the quantity of stercorine contained in the daily fæcal evacuation, and assuming that the amount of cholesterine excreted by the liver in twenty-four hours is equal to the amount of stercorine found in the evacuations, the quantity is about ten and a half grains. This corresponds with the estimates of the daily quantity of cholesterine excreted, calculated from its proportion in the bile and the estimated daily amount of bile produced by the liver.

To complete the chain of the evidence leading to the conclusion that cholesterine is an excrementitious principle, formed in certain of the tissues and eliminated by the liver, it is only necessary to show that it is liable to accumulate in the blood when the eliminating function of the liver is interrupted. It will be remembered that it was only after extirpation of the kidneys, followed by accumulation of urea in the blood, that Prévost and Dumas were able to demonstrate the preëxistence of this principle in the circulating fluid, and indicate the mechanism of its separation from the blood by the kidneys. This mode of study has been applied to certain of the elements of the bile, though without success; for Müller, Kunde, Lehmann, and Moleschott, who have extirpated the livers from frogs, looked in the blood

[1] See vol. ii., Digestion, p. 399, *et seq.*

only for the biliary salts.[1] We have not been able to repeat these experiments on frogs, and analyze the blood for cholesterine, but we have arrived at very positive results in the study of the blood in diseased conditions of the liver, that are interesting alike to the physiologist and the pathologist.

It has long been recognized that cases of ordinary icterus are not of a grave character, while there are cases in which the jaundice, though less marked as regards color, is a very different condition. Chemists have analyzed the blood, in the hope of explaining this difference by the presence, in the grave cases, of the taurocholate and glycocholate of soda; but their failure to detect these principles leaves the question still uncertain. The real distinction, arguing from purely theoretical considerations, would lie in the proposition that, in cases of simple jaundice, there is merely a resorption from the biliary passages of the coloring matter of the bile, and in grave cases—which are almost invariably fatal—there is retention of cholesterine in the blood.

We have not been able, on account of the insolubility of cholesterine, to observe the effects of injecting it into the blood-vessels, but we have had an opportunity of making an examination of the blood of a patient in the last stages of cirrhosis of the liver, accompanied with jaundice, and compared it with an examination of the blood of a patient suffering from simple icterus. Both of these patients had decoloration of the fæces; but in the first the icterus was a grave symptom, accompanying the last stages of disorganization of the liver; while in the latter it was simply dependent on duodenitis, and the prognosis was favorable and verified by the result. As icterus accompanying jaundice is of very infrequent occurrence, we were fortunate in having an opportunity of comparing the two cases.

Without giving in full the details of these cases and the examinations, which are contained in our original memoir

[1] See p. 267.

on cholesterine,[1] it is sufficient here to state the main results of the examinations of the blood and fæces.

In the case of simple jaundice from duodenitis, in which there was no great disturbance of the system, a specimen of blood, taken from the arm, presented undoubted evidences of the coloring matter of the bile, but the proportion of cholesterine was not increased, being only 0·508 of a part per thousand. The fæces contained a large proportion of saponifiable fat, but no cholesterine or stercorine.

In the case of cirrhosis with jaundice, there were ascites and great general prostration. This patient died a few days after the blood and fæces had been examined, and the liver was found in a condition of cirrhosis, with the liver-cells shrunken, and the gall-bladder contracted. In this case the blood contained 1·850 pts. of cholesterine per thousand, more than double the largest quantity we had ever found in health. The fæces contained a small quantity of stercorine.

Inasmuch as cases frequently present themselves in which there are evidences of cirrhosis of the liver, with little, if any, constitutional disturbance, while others are attended with grave nervous symptoms, it seemed an interesting question to determine whether it be possible for cholesterine to accumulate in the blood without the ordinary evidence of jaundice. We had an opportunity of examining the blood in two strongly-contrasted cases of cirrhosis, in neither of which was there jaundice.

One of these patients had been tapped repeatedly (about thirty times), but the ascites was the only troublesome symptom, and his general health was pretty good. In this case the proportion of cholesterine in the blood was only 0·246 of a part per thousand, considerably below the quantity that we had found in health.

The other patient had cirrhosis, but was confined to the bed and was very feeble. The proportion of cholesterine in

[1] *American Journal of the Medical Sciences*, Philadelphia, 1862, New Series, vol. xliv., p. 349, *et seq.*

the blood in this case was 0·922 of a part per thousand, a little above the largest proportion we had found in health.

Like the examinations of the blood in the three cases of paralysis, these pathological observations are not sufficient, in themselves, to establish the function of cholesterine; but taken in connection with our other experiments, they fully confirm our views with regard to the excretory function of the liver. It is pretty certain that organic disease of the liver, accompanied with grave symptoms generally affecting the nervous system, does not differ in its pathology from cases of simple jaundice in the fact of retention of the biliary salts in the blood; but these grave symptoms, it is more than probable, are due to a deficiency in the elimination of cholesterine—the true excrementitious principle of the bile—and its consequent accumulation in the system. Like the accumulation of urea in structural disease of the kidney, this produces blood-poisoning; and we have characterized this condition by the name of Cholesteræmia, a name expressing a pathological condition, but at the same time indicating the physiological relations of cholesterine.[1]

[1] Since this chapter has been written, numerous experiments have been made upon the relations of cholesterine to nutrition and disassimilation; but most of the observations in which attempts were made to produce toxic effects by injecting cholesterine into the blood were unsuccessful. In 1873, Koloman Müller (*Ueber Cholesterämie.—Archiv für experimentelle Pathologie und Pharmakologie*, Leipzig, 1873, Bd. i., S. 213, *et seq.*) succeeded in injecting cholesterine without any bad effects produced by mechanical obstruction of the blood-vessels. He made a preparation by rubbing cholesterine with glycerine and mixing the mass with soap and water. He injected into the veins of dogs 2·16 fluidounces of this solution, containing about 69 grains of cholesterine. In five experiments of this kind, he produced a complete representation of the phenomena of "grave jaundice." Müller's experiments are in exact accordance with our views concerning the physiological and pathological relations of cholesterine. Picot (*Journal de l'anatomie*, Paris, 1872, tome viii., p. 246, *et seq.*) has reported a fatal case of "grave jaundice," in which he determined a great increase in the proportion of cholesterine in the blood, the quantity being 1·804 per 1000.

CHAPTER X.

PRODUCTION OF SUGAR IN THE LIVER.

Evidences of a glycogenic function in the liver—Processes for the determination of sugar—Fehling's test for sugar—Examination of the blood of the portal system for sugar—Inosite—Examination of the blood of the hepatic veins for sugar—Does the liver contain sugar during life?—Characteristics of liver-sugar—Mechanism of the production of sugar in the liver—Glycogenic matter—Process for the extraction of glycogenic matter—Variations in the glycogenic function—Production of sugar in fœtal life—Influence of digestion and of different kinds of food on glycogenesis—Influence of the nervous system, etc., on glycogenesis—Artificial diabetes—Influence of the inhalation of anæsthetics and irritating vapors on glycogenesis—Destination of sugar—Alleged production of fat by the liver—Changes in the albuminoid and the corpuscular elements of the blood in their passage through the liver.

It was formerly supposed that the chief and the only important office of the liver was to produce bile, and all physiological researches into the functions of this organ were then directed to the question of the uses of the biliary secretion; but in 1848, it was announced by Bernard that he had discovered in the liver a new and important function, and he proceeded to show, by an ingeniously-conceived series of experiments, that the liver is constantly producing sugar of the variety that had long been recognized in the urine of persons suffering from diabetes mellitus. The great physiological and pathological importance of the discovery, attested, as it was, by experiments which seemed to be positively conclusive in their results, excited the most profound scientific interest. During the present century, indeed, there

have been few physiological questions that have attracted so much attention; and the observations of Bernard were soon repeated, modified, and extended by experimentalists in different parts of the world. In 1857, Bernard discovered a sugar-forming material in the liver, analogous in its composition and properties to starch; and this seemed to complete the history of glycogenesis.

Shortly after the publication of the glycogenic theory, it was found that other changes were effected in the blood in its passage through the liver, and physiologists then understood, for the first time, how glandular organs might produce secretions, and yet not discharge them into excretory ducts; and this, indeed, pointed the way to the explanation of the function of the ductless glands. It is perfectly correct to say that the liver secretes sugar; but the secretion, in this instance, is carried away by the blood; and from this point of view, the liver is a ductless gland. It is evident, therefore, that even after having studied fully the secretion and the physiological relations of the bile, we have to consider other glandular functions of the liver, hardly less important.

Evidences of a Glycogenic Function in the Liver.—The proof of the glycogenic function of the liver rests upon the fact, experimentally demonstrated by Bernard, that in all animals, the blood coming from the liver by the hepatic veins contains sugar; and that the presence of this principle here is not dependent upon the starch or sugar of the food. Bernard assumes to have proven that, in carnivorous animals, never having taken starch or sugar into the alimentary canal, except in the milk, there is no sugar in the blood of the portal vein as it passes into the liver; but, under normal conditions, the blood of the hepatic veins always contains sugar. Having examined the blood from various parts of the body, and made extracts of all the other tissues and organs, Bernard was unable to find sugar in any other situations

than the liver and the blood coming from the liver. As the blood from the liver is mixed in the vena cava with the blood from the lower extremities, and in the right side of the heart, with the blood from the descending cava, the amount of sugar is proportionately diminished in passing from the liver to the heart. It was found that the sugar generally disappeared in the lungs, and did not exist in the blood of the arterial system. Assuming that these statements have been sustained by experimental facts, there can be no doubt that the liver produces or secretes sugar; that this secretion is taken up by the blood; and that the sugar is destroyed in its passage through the lungs.

The question of the production of sugar in the economy has given rise to a great deal of discussion, and the experiments of Bernard have been repeated very extensively. Many physiologists of high authority have been able to verify these observations in every particular; but others have published accounts of experiments which seem to disprove the whole theory.

There can be no doubt of the fact that sugar may, under certain conditions, be produced *de novo* in the organism. Cases of diabetes, in which the discharge of sugar by the urine continues, to a certain extent, when no starch or sugar is taken as food, are conclusive evidence of this proposition. It is a fact equally well established, that the sugar taken as food and resulting from the digestion of starch is consumed in the organism, and is never discharged. The fact with regard to diabetes shows, then, that it is not impossible, when no sugar or starch is taken as food, that sugar should be produced in the body; and the failure to find the sugar of the food in the blood or excreta shows that this principle is normally destroyed or consumed in the organism. It only remains, therefore, to determine whether the production of sugar in diabetes be a new pathological process, or merely the exaggeration of a physiological function.

We have so often repeated and verified the observations

of Bernard, both in experiments made for purposes of investigation and in public demonstrations, that we can entertain no doubt with regard to the glycogenic function of the liver. We have, however, made some late observations, which have modified our views concerning the mechanism of glycogenesis; but the fact of the production of sugar in the healthy organism is not affected. Notwithstanding that it seems so easy to verify these experiments, there is, particularly in Great Britain, a pretty wide-spread conviction, that the liver does not produce sugar during life, and that the sugar found by Bernard and others is due to post-mortem action. This view is based chiefly on the observations of Dr. Pavy, of Guy's Hospital; but it has been adopted by some authorities in Germany and in France. In this state of the question, it will not be sufficient to detail merely the experiments that seem to demonstrate the glycogenic function, but it will be necessary to examine these observations critically, and compare them with experiments which lead, apparently, to opposite conclusions; for it is but fair to admit that the observations of Pavy seem to be as accurate, and, at the first blush, as conclusive as those of Bernard.

The experiments of Bernard were published for the first time in 1848,[1] but were afterward much extended, and published as a thesis, in 1853.[2] The most accessible account of the original experiments is in the first volume of his published lectures, delivered at the College of France, in 1854–'55.[3] In addition, many of the volumes of lectures published from time to time by Bernard contain new obser-

[1] BERNARD, *De l'origine du sucre dans l'économie animale.—Archives générales de médecine*, Paris, 1848, 4me série, tome xviii., p. 303, *et seq.*

[2] BERNARD, *Recherches sur une nouvelle fonction du foie, consideré comme organe producteur de matière sucrée chez l'homme et les animaux. Thèse présentée à la Faculté des Sciences de Paris pour obtenir le grade de Docteur ès Sciences Naturelles*, Paris, 1853.

[3] BERNARD, *Leçons de physiologie expérimentale. Cours du semestre d'hiver*, 1854–'55, Paris, 1855.

vations upon the glycogenic function;[1] and in the *Journal de la physiologie*, 1859, is an account of the formation of sugar in the fœtus,[2] followed by some reflections upon its relations to the development of the tissues.[3]

In the account of the discovery given by Bernard, it appears that he first sought for the situation in the body where the sugar derived from alimentary substances is destroyed. With this end in view, he fed a dog for seven days with articles containing a large proportion of sugar and starch. On analyzing the blood from the portal system, he found a large proportion of sugar; and he also found it in the blood of the hepatic veins. As a counter-experiment, he fed a dog for seven days exclusively on meat, and then looked for sugar in the blood of the hepatic veins; and, to his surprise, found it in abundance. This experiment he repeated frequently with the greatest care, and always with the same result; and he concluded that sugar was formed in the liver, and was contained in the blood coming from this organ independently of the diet of the animal. He afterward made extracts of the substance of the liver and of the other tissues, and found that this organ always contained sugar, while it was not to be detected in any other organ or tissue in the economy.[4] In subsequent experiments, it was demonstrated that the livers of nearly all classes of animals contained sugar, and that it existed also in the human subject.[5] He made observations, also, upon the

[1] BERNARD, *Leçons sur les effets des substances toxiques et médicamenteuses*, Paris, 1857, p. 445, *et seq.*

— *Leçons sur la physiologie et la pathologie du système nerveux*, Paris, 1858, tome i., p. 397, *et seq.*, and tome ii., p. 544, *et seq.*

— *Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme*, Paris, 1859, tome ii., p. 88, *et seq.*

[2] BERNARD, *Sur une nouvelle fonction du placenta.—Journal de la physiologie*, Paris, 1859, tome ii., p. 31, *et seq.*

[3] Idem, p. 326, *et seq.*

[4] BERNARD, *Thèse*, Paris, 1853, pp. 13, 14.

[5] BERNARD, *op. cit.*, p. 31, *et seq.* The examinations of the liver of the human subject for sugar were made by Bernard in executed criminals, soon after death,

mechanism of its production, its disappearance in the blood circulating through the lungs, and the various influences which modify the glycogenic function. These points will be considered in their appropriate place; and we will now proceed, after examining the processes for the determination of sugar, to take up, *seriatim*, the following questions:

1. The absence of sugar from the blood of the portal system in animals that have taken neither starch nor sugar into the alimentary canal.

2. The presence of sugar in the blood as it comes directly from the liver by the hepatic veins, independently of saccharine or amylaceous food.

3. The mechanism of the production of sugar by the liver.

Processes for the Determination of Sugar.—In Bernard's first observations on the liver, he applied the fermentation-test to a simple decoction of the hepatic substance, and obtained unmistakable evidences of sugar. In operating upon perfectly fresh and normal blood, the addition of water and filtration frequently sufficed to procure a clear solution, to which the ordinary copper-tests could be applied; but the most satisfactory method of making a clear extract was to boil the blood with water and an excess of sulphate of soda. By this means a clear extract can be obtained, containing, it is true, a large proportion of sulphate of soda; but this salt, fortunately, does not interfere with the tests. Later, Bernard decolorized his solutions and extracts by making the liquid into a paste with animal charcoal and filtering. We have long been in the habit of employing both of these methods; but when we have simply desired to determine the presence or absence of sugar, the process with the sulphate of soda has proved the most convenient. In delicate examinations,

and in persons killed suddenly while in perfect health. An opportunity lately occurred in Albany for the examination of the liver in a man killed suddenly. The analysis was made by the late Prof. Howard Townsend, who fully confirmed the observations of Bernard (TOWNSEND, *Glycogenic Function of the Liver*, Albany, 1864).

however, we have generally used animal charcoal. We have used both methods in decolorizing the decoction of the liver-substance, as well as in operating upon the blood.

In ordinary examinations, Trommer's test is sufficiently delicate; but it is not so sensitive nor so convenient as some of the standard test-solutions. We have been in the habit of using, for the determination of sugar in the urine, a modification of Fehling's test, which is also very convenient for examinations of the blood and liver-extract. This may also be used for quantitative examinations; but, like all of the standard solutions, it presents the inconvenience of undergoing alteration by keeping, so that it is desirable to use it freshly-made for each series of examinations. We have succeeded in obviating this difficulty, however, by the following modification in its preparation; and, made in this way, it is probably the most convenient test that can be used in the examination of any of the animal fluids for sugar.

Fehling's Test for Sugar.—The modification in the test consists simply in preparing three separate solutions, which are to be mixed just before using, as follows:

Solution of crystallized sulphate of copper, **94·73 grains** in an ounce of distilled water.

Solution of neutral tartrate of potash, 378·91 grains in an ounce of distilled water.

Solution of caustic soda, specific gravity 1·12.

These solutions are to be kept in separate bottles, and used as follows:

Take half of a fluidrachm of the copper-solution, add half a fluidrachm of the tartrate of potash, add fifteen minims of distilled water, and add the caustic soda, to make three fluidrachms. It is important to measure the copper-solution with accuracy, in quantitative analyses, as the quantity of copper decomposed indicates the amount of sugar.[1]

[1] The above modification of Fehling's test consists simply in making and keeping the solutions separately, and mixing them for use in the proportions

To apply this test in ordinary qualitative analyses, heat a small portion of the test-liquid to the boiling point in a test-tube, and add the suspected fluid, drop by drop. If sugar be present in even a moderate quantity, a dense yellowish precipitate of the suboxide of copper will be produced after adding a few drops; and if the liquid be added to about the same volume as the test, and the mixture be again raised to the boiling point, without producing any deposit, it is certain that no sugar is present. The estimation of the quantity of sugar in any liquid depends upon the fact that two hundred grains of the test-liquid is decolorized by exactly one grain of glucose. To apply this test, measure off in a glass, specially graduated for the purpose, two hundred grains of the solution; put this into a flask, with about twice its volume of distilled water, and boil; when boiling, add the suspected solution, little by little, from a burette graduated in grains (raising the mixture to the boiling point each time and afterward allowing the precipitate to subside), until the blue color is completely discharged; by then reading off the number of grains of the saccharine solution that has been added, the proportion of sugar may be readily calculated. If the solution be suspected to contain a considerable quantity of sugar, the estimate may be more accurately made by diluting it to a known degree, say with nine parts of water, and adding this diluted mixture to the test-liquid.

Bernard, in his quantitative examinations, employed a test-liquid known as Barreswil's solution, but the process is essentially the same as the one we have just described. One advantage of boiling the standard liquid before applying the

required. The formula given by Roberts is adapted to the imperial measure; reduced to English grains and wine-measure, it is as follows:

> Sulphate of copper, 94·73 grains;
> Neutral tartrate of potash, 378·91 grains;
> Solution of caustic soda, sp. gr. 1·12, three and a half fluidounces.
> Add water to make exactly six fluidounces.

—(ROBERTS, *Urinary and Renal Diseases*, Philadelphia, 1866, p. 147. The error made by Roberts in taking the volume instead of the weight of the soda-solution has also been corrected. These corrections were suggested by Dr. Thomas Ryerson, of Newton, N. J.)

test is that, when it is altered so as to be unreliable, the yellow precipitate is thrown down by simple boiling. In making delicate examinations, it is best always, when this occurs, to make a fresh solution.[1]

Examination of the Blood of the Portal System for Sugar.—If starch or sugar be taken into the alimentary canal, it is well known that sugar is always to be found, during absorption, in the blood of the portal system; but in the carnivorous animals, that have been fed entirely upon meat, no sugar is to be found in the portal blood. Bernard is very definite upon this point, and indicates a liability to error when the operation of tying the portal vein has not been skilfully performed, and when blood, containing sugar, is allowed to regurgitate from the substance of the liver. In taking the blood just before it enters the liver, it is necessary to apply a ligature to the vessels as they penetrate at the transverse fissure. This should be done quickly, and the opening into the abdominal cavity should be small. Otherwise, as the vessels have no valves, we are liable to have reflux of blood from the liver. We have frequently performed the experiment, after the method described by Bernard, making a small opening in the linea alba a little below the ensiform cartilage, just large enough to admit the forefinger of the left hand; introducing the finger, and feeling along the concave surface of the liver until we are able to seize the vessels; then passing in an aneurism-needle, and constricting the vessels before the abdomen is widely opened, when a firm ligature is applied. When this step of the operation has been satisfactorily performed, we have never found a trace of sugar in the extract from the blood of the portal system, in animals that have been fed upon nitrogenized matter alone.

Among those who have refused to admit the glycogenic

[1] The properties of the test-liquid may be restored sufficiently for ordinary qualitative examinations by adding a little more caustic soda and filtering.

function of the liver, there have been few who have denied the proposition that the portal blood does not contain sugar except during absorption of this principle from the alimentary canal. Figuier, who made an elaborate series of investigations on this subject with the view of invalidating the experiments of Bernard, assumed that this proposition was incorrect, and that the portal blood carries sugar to the liver during the digestion of starchy and saccharine matters, where it is retained,[1] and, farthermore, that there is sugar in the blood of the portal vein during the digestion of raw meat.[2] From these and other observations, Figuier concludes that the liver does not produce sugar, but that the sugar, brought to this organ by the portal blood, is here stored up, to be passed, little by little, into the blood of the hepatic veins.[3]

These conclusions cannot be accepted, for the reason that the evidence of the presence of sugar in the portal blood of animals during the digestion of meat is far from satisfactory. A commission of the French Academy of Sciences, composed of MM. Dumas, Pelouze, and Rayer, after a careful examination of the extracts of the portal blood presented by M. Figuier, decided that the evidence of the presence of sugar was insufficient, and came to the conclusion "that sugar was not appreciable in the blood of the portal vein of a dog fed on raw meat."[4] This seems to settle the question, as far as the observations of M. Figuier are concerned, the report of the commission being pretty generally accepted as conclusive.[5]

[1] Figuier, *Mémoire sur l'origine du sucre dans le foie et sur l'existence normale du sucre dans le sang de l'homme et des animaux.—Comptes rendus*, Paris, 1855, tome xl., p. 228.

[2] Figuier, *Deuxième mémoire à propos de la fonction glycogénique du foie.—Comptes rendus*, Paris, 1855, tome xl., p. 674.

[3] Figuier, *Troisième mémoire sur la fonction glycogénique du foie.—Comptes rendus*, Paris, 1855, tome xli., p. 352.

[4] Dumas, *Rapport sur divers mémoires relatifs aux fonctions du foie.—Comptes rendus*, Paris, 1855, tome xl., p. 1281.

[5] Bérard, *Note additionnelle au mémoire lu à l'Académie dans la séance du 1[?] mai*, 1857.—*Gazette hebdomadaire*, Paris, 1857, tome iv., p. 414.

The only other question that has been raised with regard to the possible presence of sugar or sugar-forming matter in the blood of the portal vein has been that inosite ($C_{12}H_{12}O_{12}$), a substance discovered by Scherer in the muscular tissue of the heart,[1] might be introduced into the portal blood with the animal food. But even if inosite should be contained in food and be detected in the blood of the portal system, it cannot possibly have any thing to do with the glycogenic process, and it is not known that it has any relations to the sugars. Anhydrous inosite is isomeric with anhydrous glucose, but it does not respond to any of the copper-tests, and is unfermentable.[2]

In view of all these facts, there can be no doubt that the blood carried to the liver by the portal vein does not contain sugar, in animals fed solely upon nitrogenized matters. The quantity of blood carried to the liver by the hepatic artery is insignificant; and, although the arterial blood may temporarily contain a trace of sugar, as we shall see farther on, this need not complicate the question under consideration, as the presence of sugar in the blood of the hepatic artery is exceptional, and its proportion, when it exists, is very minute.

Examination of the Blood of the Hepatic Veins for Sugar.—It is upon this question that the whole doctrine of the sugar-producing function of the liver must rest. If it can be proven that the blood, taken from the hepatic veins during life or immediately after death, normally contains sugar, while the blood distributed to the liver contains neither sugar nor any substance that can be immediately converted into sugar, the inevitable conclusion is that the liver is a sugar-producing organ. We shall, consequently, examine this part of the question with the care which its importance demands.

[1] SCHERER, *Ueber eine neue, aus dem Muskelfleische, gewonnene Zuckerart.—Annalen der Chemie und Pharmacie*, Heidelberg, 1850, Bd. lxxiii., S. 322, *et seq.*

[2] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 264.

The proposition that the blood from the hepatic veins does not contain sugar during life and health cannot be sustained by actual experiment. Observers may say that the quantity is very slight, but its existence in this situation, independently of the kind of food taken, cannot be denied. Dr. Pavy, who is the originator of the theory that the sugar found in the liver and in the blood coming from the liver is due to a post-mortem change, nowhere states that he has taken the blood from the hepatic veins and failed to find sugar. He states that he has found the blood taken from the right side of the heart by catheterization, in a living animal, "scarcely at all impregnated with saccharine matter,"[1] but he does not deny its presence in small quantity. In twelve examinations made by Dr. M'Donnell, of Dublin, traces of sugar were found in five specimens of blood taken from the right auricle by catheterization, in the living animal, and no sugar was detected in seven.[2] It must be remembered, in considering these experiments, that the blood of the right side of the heart is the mixed blood from the entire body; and, assuming that the hepatic blood is constantly saccharine, the quantity in the blood of the right heart would not be very great.

In opposition to these experiments, which are only partially negative, we have the following results of examinations of the blood of the hepatic veins and of the right side of the heart taken as nearly as possible under normal conditions.

To demonstrate the absence of sugar in the portal vein and its constant presence in the hepatic veins in dogs fed exclusively on meat, Bernard employed the following process: The animal was killed instantly by section of the medulla oblongata. A small opening was then made into the abdomen, just large enough to admit the finger and to enable

[1] Pavy, *Researches on the Nature and Treatment of Diabetes*, London, 1862, pp. 44, 46.

[2] M'Donnell, *Observations on the Functions of the Liver*, Dublin, 1865, p. 4.

him to seize the portal vein as it enters at the transverse fissure, and apply a ligature. The abdomen was then freely opened and a ligature applied to the vena cava just above the renal veins, to shut off the blood from the posterior extremities. The chest was then opened, and a ligature was applied to the vena cava just above the opening of the hepatic veins. Operating in this way, blood may be taken from the portal system before it enters the liver, and from the hepatic veins as it passes out. In the blood from the portal system no sugar is to be found, but its presence is unmistakable in the blood from the hepatic veins.[1] To avoid disturbing the circulation in the liver, and in order to collect from the hepatic veins as large a quantity of blood as possible, Bernard modified the experiment, in some instances, by introducing into the vena cava in the abdomen a double sound, the extremity of which is provided with a bulb of India-rubber. This was pushed into the vein above the diaphragm; and by inflating the bulb, the vein was obstructed above the liver, and the blood could be collected through one of the canulæ, as it came directly from the hepatic vessels. Bernard never failed to determine the presence of sugar in these specimens of blood, employing a number of different processes, including the fermentation-test and even collecting the alcohol.[2] To complete the proof of the existence of sugar in the blood coming from the liver, Bernard demonstrated its presence in blood taken from the right auricle in a living animal. He also showed that during digestion the whole mass of blood contained sugar, but the quantity was greater in the right side of the heart than in the arterial system.[3]

It is unnecessary to cite all the authorities that have confirmed the observations of Bernard. Shortly after these

[1] BERNARD, *Recherches sur une nouvelle fonction du foie*, Paris, 1853, p. 56.

[2] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 494 The reader will find here a description, with a figure, of the instrument mentioned in the text, which is very ingenious.

[3] *Op. cit.*, p. 120.

experiments were published, Lehmann,[1] Frerichs,[2] and many others verified their accuracy. Bernard gives in full the experiments of Poggiale[3] and of Leconte,[4] the results of which were identical with his own. He gives, also, in one of his later works, the proportions of sugar in the blood of the hepatic veins, obtained by Lehmann, Schmidt, Poggiale, and Leconte; no sugar being found in the blood of the portal system.[5] We have ourselves made a number of experiments with a view of harmonizing, if possible, the discordant observations of Bernard and Pavy, and have examined the blood from the hepatic veins for sugar, taking the specimens under what seemed to be strictly physiological conditions. In one of these published experiments, blood was taken from the hepatic veins of a large dog, fully-grown and fed regularly every day, but not in digestion at the time of the experiment, and the operation lasted only seventy seconds. No anæsthetic was employed. The extract of this specimen of blood, treated with Fehling's test-liquid, presented a well-marked deposit of the oxide of copper, revealing unequivocally the presence of a small quantity of sugar.[6] This has been the invariable result in numerous experiments and class-demonstrations made since 1858; and since the experiments just referred to were published, we have verified the observation with regard to the hepatic blood, keeping the animal perfectly quiet before the opera-

[1] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 257.

[2] FRERICHS, *Verdauung.*—WAGNER'S *Handwörterbuch der Physiologie*, Braunschweig, 1846, Bd. iii., erste Abtheilung, S. 831.

[3] POGGIALE, *La matière sucrée se forme-t-elle par l'action digestive, dans le foie et dans le torrent circulatoire?* in BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 497.

[4] LECONTE, *Recherches sur la fonction glucogénique du foie*, Idem, p. 499.

[5] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 98.

[6] FLINT, JR., *Experiments undertaken for the Purpose of reconciling some of the Discordant Observations upon the Glycogenic Function of the Liver.*—*New York Medical Journal*, 1869, vol. viii., p. 381. These experiments will be referred to again in treating of the question of the existence of sugar in the substance of the liver during life.

tion, avoiding the administration of an anæsthetic, and taking the blood so rapidly that no sugar could be formed by the liver post mortem. These experiments leave no doubt of the fact that, during life and in health, the blood, as it passes through the liver and is discharged by the hepatic veins into the vena cava, contains sugar, which is formed by the liver, independently of the sugar and starch taken as food.

Does the Liver contain Sugar normally during Life?—This is the only question upon which the results of reliable experiments have been entirely opposite. Bernard made the greater part of his observations by analyzing the substance of the liver; and he arrived at most of his conclusions with regard to the variations in the glycogenic function, from estimates of the proportion of sugar in the liver under different conditions. For many years we have been in the habit of repeating these experiments, with like results, and never failed to find sugar, under normal conditions of the system. We were formerly in the habit of making the demonstrations of the formation of sugar in the liver upon animals that had been etherized; and then we always obtained a brilliant precipitate from the clear extract of the substance of the liver boiled with the test-liquid. The experiment was performed in this way before we had acquired sufficient dexterity to seize the portal vein readily and to go through with the necessary manipulations with rapidity. We subsequently made the operation by first suddenly breaking up the medulla oblongata, then making a small incision into the abdominal cavity, seizing the portal vein instantly, and following out the remaining steps of the experiment without delay. In this way, although sugar was always found in the blood of the hepatic veins, we frequently failed to obtain a distinct reaction in the extract of the liver; and it seemed, indeed, that the more accurately and rapidly the operation was performed, the more difficult was it to detect sugar in the hepatic substance.

It seems probable, in reflecting upon these facts, that, inasmuch as no one has assumed that the actual quantity of sugar produced by the liver is very considerable, and as a large quantity of blood (in which the sugar is very soluble) is constantly passing through the liver, precisely as we pass water through its vessels to remove the sugar, the sugar might be washed out by the blood as fast as it is formed; and really the liver might never contain sugar in its substance, as a physiological condition, although it is constantly engaged in its production. We know that the characteristic elements of the various secretions proper are produced in the substance of the glands, and are washed out at the proper time by liquid derived from the blood, which circulates in their substance during their functional activity in very much greater quantity than during the intervals of secretion. Now, the liver-sugar may certainly be regarded as an element of secretion; and, possibly, it may be completely washed out of the liver, as fast as it is formed, by the current of blood; the hepatic vein, in this regard, serving as an excretory duct.

To put this hypothesis to the test of experiment, it was necessary to obtain and analyze a specimen of the liver in a condition as near as possible to that under which it exists in the living organism; and in carrying out this idea, we instituted the following experiments:

Experiment I.—A medium-sized dog, full-grown, in good condition, not in digestion, was held upon the operating-table by two assistants, and the abdomen was widely opened by a single sweep of the knife. A portion of the liver, weighing about two ounces, was then excised and immediately cut into small pieces, which were allowed to fall into boiling water. The time from the first incision until the liver was in the boiling water was twenty-eight seconds. An excess of crystallized sulphate of soda was then added, and the mixture was boiled for about five minutes. It was then thrown upon a filter, and the clear fluid

that passed through was tested for sugar by Trommer's test. The reaction was doubtful, and presented no marked evidence of sugar.

Experiment II.—A medium-sized dog, in the same condition as the animal in the first experiment, was held upon the table, and a portion of the liver excised, as above described. The whole operation occupied twenty-two seconds. But ten seconds elapsed from the time the portion of the liver was cut off until it was in the boiling water. It was boiled for about fifteen minutes, made into a paste with animal charcoal, and thrown upon a filter. The clear fluid that passed through was tested for sugar by Trommer's test. There was no marked evidence of sugar.

Experiment III.—A large dog, full-grown, and fed regularly every day, but not in digestion at the time of the experiment, was held firmly upon the table. This dog had been in the laboratory about a week, and was in a perfectly normal condition. The abdominal cavity was opened, and a piece of the liver cut off and thrown into boiling water, the time occupied in the process being ten seconds. Before the liver was cut up into the boiling water, the blood was rinsed off in cold water. The liver was boiled for about seventeen minutes, mixed with animal charcoal, and the whole thrown upon a filter.

Immediately after cutting off a portion of the liver and throwing it into boiling water, the medulla oblongata was broken up; a ligature was applied to the ascending vena cava, just above the renal veins; the chest was opened, and a ligature applied to the vena cava, just above the opening of the hepatic veins. A specimen of blood was then taken from the hepatic veins. This portion of the operation occupied not more than one minute. A little water was added to the blood, which was boiled briskly, mixed with animal charcoal, and thrown upon a filter. The liquid that passed through from both specimens was perfectly clear.

While the filtration was going on, Fehling's test-liquid

was made up, so as to be perfectly fresh. The two liquids were then carefully tested for sugar. The extract of the liver presented not the slightest trace of sugar. The extract from the blood of the hepatic veins presented a well-marked deposit of the oxide of copper, revealing unequivocally the presence of a small quantity of sugar.

Experiment IV.—This experiment was made upon a medium-sized dog, in full digestion of meat. The medulla oblongata was broken up; the portal vein was tied through a small opening in the abdomen; and the abdomen was then widely opened, and a portion of the liver excised, rapidly rinsed, and cut up into boiling water. The length of time that elapsed between breaking up the medulla and cutting up the specimen of liver into the boiling water was one minute.

The vena cava was then tied above the renal veins, the chest opened, and the cava again tied above the hepatic veins. Blood was then taken from the hepatic veins, about an equal bulk of water was added with an excess of the crystallized sulphate of soda, and the mixture was boiled. A portion of the portal blood and the decoction of the liver were then treated in the same way, and the three specimens filtered.

The clear extracts were then tested with Fehling's liquid, with the following result:

There was no sugar in the portal blood.

There was no sugar in the extract of the liver.

There was a marked reaction in the extract of the blood from the hepatic veins, the precipitate rendering the whole solution bright yellow and entirely opaque.

This experiment was made in the presence of the class, at the Bellevue Hospital Medical College, January 4, 1869.

The importance of the question under consideration and its present unsettled condition are, we hope, sufficient to justify the introduction of the details of the preceding experiments. They were undertaken with the view of har-

monizing, if possible, the facts brought forward by different experimentalists.

It is difficult to imagine how any observer, so well known and accurate as Dr. Pavy, could assert positively, as the result of personal examination, that the liver does not contain sugar when examined immediately after its removal from the living body, when Bernard and so many others have demonstrated its presence in this organ in large quantity. Yet such was the result of all the experiments of Pavy,[1] and the same conclusion was arrived at by M'Donnell,[2] and afterward by Meissner and Jaeger, and by Schiff.[3] The elegant experiment of Bernard, showing that sugar is formed in a liver removed from the body and washed sugar-free by a stream of water passed through its vessels,[4] demonstrated the possibility of the production of sugar post mortem, so strongly claimed by Pavy as the only condition under which it is ever formed; still, it does not seem possible to deny the sugar-producing function of the liver, in view of the conclusive experimental proof of the constant presence of glucose in the blood of the hepatic veins.

From our own experiments we have come to the conclusion that Dr. Pavy and those who adopt his views cannot consistently deny that sugar is constantly formed in the liver

[1] PAVY, *Researches on Sugar Formation in the Liver.—Philosophical Transactions*, London, 1860, p. 595, and *Researches on the Nature and Treatment of Diabetes*, London, 1862, p. 52, *et seq.*

[2] M'DONNELL, *Observations on the Functions of the Liver*, Dublin, 1865, p. 4, *et seq.*

[3] SCHIFF, *Nouvelles recherches sur la glycogénie animale.—Journal de l'anatomie*, Paris, 1866, tome iii., p. 354, *et seq.* Meissner and Jaeger and Schiff took portions of the liver from living animals and from animals at the instant they were killed by section of the medulla oblongata, plunged the tissue immediately into boiling water, and invariably failed to find sugar in the extract. They did not, however, recognize sugar in the blood coming from the liver, as we did in our own experiments.

[4] BERNARD, *Sur le méchanisme de la formation du sucre dans le foie.—Comptes rendus*, Paris, 1855, tome xli., p. 461, and *Leçons sur les effets des substances toxiques et médicamenteuses*, Paris, 1857, p. 453.

and discharged into the blood of the hepatic veins; nor can Bernard and his followers ignore the fact that the liver does not contain sugar during life; although, as has been shown by Pavy, and more specifically by M'Donnell,[1] sugar appears in the liver in great abundance soon after death.

In the experiments that we have just detailed, which are simply typical examples of numerous unrecorded observations, we attempted to verify the observations of Pavy without losing sight of the facts observed by Bernard, and to verify the experiments of Bernard in the face of the apparently contradictory statements of Pavy. When an animal is in perfect health, has been kept quiet before the experiment, and a piece of the liver is taken from him by two sweeps of the knife, the blood rinsed from it and the tissue cut up into water already boiling, the whole operation occupying only ten seconds (as was the case in Experiment III.), the liver is as nearly as possible in the condition in which it exists in the living organism. As this was done repeatedly in animals during digestion and in the intervals of digestion, and an extract thoroughly made without finding any sugar, we regarded the experiments of Pavy as entirely confirmed, and the fact demonstrated that the liver does not contain sugar during life. On the other hand, when we made the experiment on the liver as above described, and, in addition, took specimens of the portal blood and the blood from the hepatic veins, under strictly physiological conditions (as was done in Experiment IV.), and found no sugar in the portal blood or in the substance of the liver, but an abundance in the blood of the hepatic veins, it was impossible to avoid the conclusion that the sugar was formed in the liver, and was washed out in the blood as it passed through.

In treating of the mechanism of the formation of sugar in the liver, we shall describe more fully the glycogenic matter; but, taking into consideration the demonstration of the

[1] *Loc. cit.*

presence of sugar in the blood of the hepatic veins by Bernard; his discovery of the post-mortem production of sugar in a liver washed sugar-free, probably from a substance remaining in the liver and capable of being transformed into sugar; the negative results of the examinations of the liver for sugar by Pavy; and, adding to this our own experiments upon all of these points, we are justified in adopting the following conclusions:

1. A substance exists in the healthy liver, which is capable of being converted into sugar; and inasmuch as this is formed into sugar during life, the sugar being washed away by the blood passing through the liver, it is perfectly proper to call it glycogenic, or sugar-forming matter.

2. The liver has a glycogenic function, which consists in the constant formation of sugar out of the glycogenic matter, this being carried away by the blood of the hepatic veins, which always contains sugar in a certain proportion. This production of sugar takes place in the carnivora, as well as in those animals that take sugar and starch as food; and it is, essentially, independent of the kind of food taken.

3. During life, the liver contains only the glycogenic matter and no sugar, because the great mass of blood which is constantly passing through this organ washes out the sugar as fast as it is formed; but after death, or when the circulation is interfered with, the transformation of glycogenic matter into sugar goes on; the sugar is not removed under these conditions, and can then be detected in the substance of the liver.

Characteristics of the Liver-Sugar.—Very little is to be said regarding the chemical peculiarities of liver-sugar. It resembles glucose, or the sugar resulting from the digestion of starch, in its composition, having for its formula, in a crystalline form, $C_{12}H_{14}O_{14}$. The formula for the anhydrous sugar is $C_{12}H_{12}O_{12}$. This sugar, like glucose, responds promptly to all of the copper-tests, and undergoes trans-

formation into melassic acid on being boiled with an alkali. One of its most marked peculiarities is that it ferments more readily than any other variety of sugar; and another peculiarity, described first by Bernard, is that it is destroyed in the economy with extraordinary facility. This fact has been illustrated by the following ingenious experiment: Bernard injected under the skin of a rabbit a little more than seven grains of cane-sugar, dissolved in about an ounce of water, and found sugar in the urine. Under the same conditions, he found he could inject seven grains of milk-sugar, fourteen and a half grains of glucose, twenty-one and a half grains of diabetic sugar, and nearly thirty grains of liver-sugar, without finding any sugar in the urine;[1] showing that the liver-sugar is consumed in the organism more rapidly and completely than any other saccharine principle.

Mechanism of the Production of Sugar in the Liver.—When Bernard first described the glycogenic function of the liver, he thought that the sugar was produced from nitrogenized principles, in some manner which he did not attempt to explain.[2] Subsequent discoveries, however, have led to conclusions entirely different.

In 1855, Bernard first published an account of his remarkable experiment showing the post-mortem production of sugar. After washing out the liver with water passed through the vessels, until it no longer contained a vestige of sugar, it was allowed to remain at about the temperature of the body for a few hours, and was then found to contain sugar in abundance.[3] This experiment we have already referred to, and it is one that we have frequently verified. Bernard explained the phenomenon by the supposition, sub-

[1] Bernard, *Leçons de physiologie expérimentale*, Paris, 1855, p. 214.

[2] Bernard, *Recherches sur une nouvelle fonction du foie*, *Thèse*, Paris, 1853, p. 77.

[3] Bernard, *Sur le méchanisme de la formation du sucre dans le foie.—Comptes rendus*, Paris, 1855, tome xli., p. 461.

sequently shown to be correct, that the liver contains a peculiar principle, slightly soluble in water and capable of transformation into sugar. We have given rather a detailed account of this observation, because some authors have attributed the discovery of the glycogenic matter to Hensen. Hensen confirmed Bernard's observations, in 1856, and described the insoluble substance rather more fully.[1] In 1857, Bernard studied the mechanism of the glycogenic function more closely, and completed his description of the glycogenic matter.[2]

Glycogenic Matter ($C_{12}H_{12}O_{12}$).—In its composition, reactions, and particularly in the facility with which it undergoes transformation into sugar, glycogenic matter bears a very close resemblance to starch. It is described by Pavy under the name of amyloid matter,[3] a name which is applied to it, also, by Rouget.[4] It is insoluble in water, and, by virtue of this property, may be extracted from the liver after the sugar has been washed out. The following is the method for its extraction proposed by Bernard:[5]

The liver of a small and young animal, like the rabbit, in full digestion, presents the most favorable conditions for the extraction of the glycogenic matter. The liver is taken from the animal immediately after it is killed, is cut into thin slices, and thrown into boiling water. When the tissue is hardened, it is removed and ground into a pulp in a mortar. It is then boiled a second time in the water of the

[1] HENSEN, *Ueber die Zuckerbildung im thierischen Organismus.*—SCHMIDT'S *Jahrbücher*, Leipzig, 1857, Bd. xciii., S. 15; taken from *Verhandlungen der phy.-med. Ges. zu Würzb.*, 1856, Bd. vii., S. 219.

[2] BERNARD, *Sur le méchanisme physiologique de la formation du sucre dans le foie.—Comptes rendus*, Paris, 1857, tome xliv., p. 578.

[3] PAVY, *Researches on the Nature and Treatment of Diabetes*, London, 1862, p. 26, *et seq.*

[4] ROUGET, *Des substances amyloïdes; de leur rôle dans la constitution des tissus des animaux.—Journal de la physiologie*, Paris, 1859, tome ii., pp. 83, 308. Rouget calls the glycogenic matter, or animal starch, zoamyline.

[5] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 119.

first decoction, strained through a cloth, and the opaline liquid

FIG. 12.

which passes through is made into a thin paste with animal charcoal. 'The paste is then put into a displacement apparatus, the end of which is loosely filled with shreds of moistened cotton. By successive washings, the paste is exhausted of its glycogenic matter, leaving behind the albuminoid and coloring matters. The whitish liquid, as it flows, is received into a vessel of absolute alcohol, when, as each drop falls, the glycogenic matter is precipitated in great, white flakes. This is filtered and dried rapidly in a current of air. If the alcohol be not allowed to become too dilute, the matter when dried is white and easily pulverized. The apparatus used by Bernard is represented in Fig. 12: A B, displacement apparatus in which the filtration takes place; C, animal charcoal mixed with the decoction of the liver; E, glycogenic solution; M, lamp-wicking, attached to a thread, passing through the carbon, and coming out at the upper part of the apparatus; I, precipitating-glass; G, glycogenic matter precipitated; V, alcohol.'[1] The substance thus obtained may be held in suspension in water, giving to the liquid a strongly

[1] BERNARD, *op. cit.*, p. 120.

opaline appearance. It is neutral, without odor or taste, and presents nothing characteristic under the microscope. It reacts strongly with iodine, which produces a dark-violet or chestnut-brown color, but rarely a well-marked blue. It presents none of the reactions of sugar, and is entirely insoluble in alcohol.[1] It is changed into sugar by boiling for a long time with dilute acids, and this conversion is rapidly effected by the saliva, the pancreatic juice, and a peculiar ferment found in the substance of the liver. Prepared in the way above indicated, and pulverized, it may be preserved for an indefinite period.

The peculiar reaction of the glycogenic matter with iodine has led to its recognition in the substance of the liver-cells and in some other situations. Schiff found in the liver-cells minute granulations, which presented the peculiar color on the addition of iodine, characteristic of glycogenic matter.[2] Bernard, a few years after his discovery of this principle in the liver, recognized it in cells attached to the placenta. He believes that these cells produce sugar during the early period of fœtal life, before the liver takes on this function, and that they disappear during the later months, as the liver becomes fully developed.[3]

Since the discovery of the glycogenic function of the liver, anatomists have found amyloid corpuscles in various of the tissues of the body. We do not propose, however, to discuss this question in all its bearings, but only to consider the known relations of the amyloid substances found in the body to the formation of sugar.

In the first place, there can be no doubt of the fact, that the liver of a carnivorous animal that has been fed exclusively on meat contains an amyloid substance readily con-

[1] BERNARD, *Leçons sur la physiologie et la pathologie du système nerveux*, Paris, 1858, tome i., p. 470.

[2] SCHIFF, *De la nature des granulations qui remplissent les cellules hépatiques: Amidon animale.—Comptes rendus*, Paris, 1859, tome xlviii., p. 880.

[3] BERNARD, *Sur une nouvelle fonction du placenta.—Journal de la physiologie*, Paris, 1859, tome ii., p. 31, *et seq.*

vertible into sugar. The experiments of Bernard, of Pavy, and all, indeed, agree upon this point. The question of the existence of the same amyloid matter in other tissues and organs is only pertinent in so far as it bears upon the production of sugar or upon the formation of the glycogenic matter in the liver. In no tissue or organ in the adult has it been demonstrated that there is any formation of sugar, except the ordinary transformation of starch into sugar in the process of digestion; but it has been claimed that amyloid matter is contained in the flesh of herbivorous animals, and is taken up by the carnivora and deposited in the liver. M. Sanson has made two elaborate communications on this subject, and concludes, from his own experiments, that the liver has no glycogenic function.[1] These experiments were repeated by M. Sanson in the presence of a commission from the French Academy of Medicine, composed of MM. Bouley, Poggiale, and Longet, and were reported upon to the Academy. The conclusions of the commission were unreservedly in favor of the glycogenic function of the liver; and out of a great number of observations, in only one was any amyloid matter discovered in butcher's meat.[2] It was found normally in horse-flesh, and, as subsequent experiments showed, could be produced in the muscular tissue of various of the herbivora, by feeding them upon certain articles, particularly oats and barley.[3]

If the liver taken from an animal freshly killed be simply kept at about the temperature of the body, after it has been drained of blood, or even after it has been washed through the vessels, sugar will be rapidly formed in its substance.

[1] SANSON, *De l'origine du sucre dans l'économie animale.—Journal de la physiologie*, Paris, 1858, tome i., p. 244, *et seq.*, and *Sur l'existence de la matière glycogène dans tous les organes des herbivores et sur l'influence de l'alimentation sur la production de cette substance.—Journal de la physiologie*, Paris, 1859, tome ii., p. 104, *et seq.*

[2] POGGIALE, *Sur la formation de la matière glycogène dans l'économie animale.—Journal de la physiologie*, Paris, 1858, tome i., p. 549, *et seq.*

[3] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome ii., p. 111

This must be due to some ferment remaining in the tissue; and Bernard has, indeed, been able to isolate a principle which exerts this influence in a marked degree. If an opaline decoction of the liver be allowed to stand until it has become entirely clear, showing that all the glycogenic matter has been transformed into sugar, and alcohol be added to the liquid, the hepatic ferment will be precipitated. This may be redissolved in water, and it effects the transformation of starch into sugar with great rapidity.[1]

From these facts it is pretty conclusively shown that the following is the mechanism of the production of sugar in the liver:

The liver first produces a peculiar principle, analogous to starch in its composition and in many of its properties, though it contains two atoms more of water, out of which the sugar is to be formed. The name, glycogenic matter, may properly be applied to this substance. It is, as far as is known, produced in all classes of animals, carnivora and herbivora; and though its quantity may be modified by the kind of food, its formation is essentially independent of the alimentary principles absorbed.

The glycogenic matter is not taken up by the blood as it passes through the liver, but is gradually transformed, in the substance of the liver, into sugar, which is washed out of the organ as fast as it is produced. Thus the blood of the hepatic veins always contains sugar, though sugar is not contained in the substance of the liver during life.

Variations in the Glycogenic Function.

In following out the relations of the glycogenic process to the various animal functions, Bernard studied very closely its variations at different periods of life, with digestion, the influence of the nervous system, and other modifying conditions. He made some of his observations by examining the

[1] BERNARD, *op. cit.*, p. 124.

blood in living animals, and others, by estimating the proportion of sugar in the liver. The latter method must be considered, with an appreciation of the fact that the liver does not normally contain sugar during life; but it represents, to a certain extent, the activity of the glycogenic function. Still, the facts arrived at in this way must be taken with a certain degree of caution.

Glycogenesis in the Fœtus.—In the early months of fœtal existence, many of the tissues and fluids of the body were found by Bernard to be strongly saccharine; but at this time no sugar is to be found in the liver. Taking the observations upon fœtal calves as the criterion, sugar does not appear in the liver until toward the fourth or fifth month of intra-uterine life.[1] Before this period, however, epithelial cells filled with glycogenic matter are found in the placenta, and these produce sugar until the liver takes on its functions. As the result of numerous observations by Bernard upon fœtal calves, this function of the placenta appears very early in fœtal life, and, at the third or fourth month, has attained its maximum. At about this time, when glycogenic matter begins to appear in the liver, the glycogenic organs of the placenta become atrophied, and are lost some time before birth.[2]

Influence of Digestion, and of Different Kinds of Food.—Activity of the digestive organs has a marked influence upon the production of sugar in the liver. In a fasting animal, sugar is always found in the blood of the hepatic veins and in the vessels between the liver and the heart, but it

[1] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 82.

[2] BERNARD, *Sur une nouvelle fonction du placenta.*—*Journal de la physiologie*, Paris, 1859, tome ii., p. 33. Bernard found glycogenic matter in the placenta of animals in which the organ was single, as in the human subject; but in animals with multiple placenta he did not at first discover the glycogenic organs, which he subsequently found, not in the vascular portion, but attached to the amnion.

never passes the lungs, and does not exist in the arterial system. During digestion, however, even when the diet is entirely nitrogenized, the production of sugar is so much increased that a small quantity frequently escapes decomposition in the lungs, and passes into the arterial blood.[1] Under these conditions, the quantity in the arterial blood is sometimes so large that a trace may appear in the urine, as a temporary and exceptional, but not an abnormal condition. This physiological fact is well illustrated in certain cases of diabetes. There are instances, indeed, in which the sugar appears in the urine only during digestion;[2] and in almost all cases, the quantity of sugar eliminated is largely increased after eating. Pavy mentions a very striking instance of this kind, in which the examinations of the urine were made with great care.[3]

The influence of the kind of food upon the glycogenic function is a question of great pathological as well as physiological importance. It is well known to pathologists that certain cases of diabetes are relieved when the patient is confined strictly to a diet containing neither saccharine nor amylaceous principles,[4] and that, almost always, the quantity of sugar discharged is very much diminished by such a course of treatment; but there are instances in which the discharge of sugar continues, in spite of the most carefully-regulated diet. Bernard does not recognize fully the influence of different kinds of food upon glycogenesis, and his experiments on this point are wanting in accuracy, from the fact that the proportion of sugar in the liver is given, without indicating at what period after death the examinations were made. In the observations on this point by Pavy, the examinations of

[1] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 111.

[2] BERNARD, *op. cit.*, p. 114.

[3] PAVY, *Researches on the Nature and Treatment of Diabetes*, London, 1862, p. 142.

[4] Several very striking examples of this kind are given by Pavy (*op. cit.*, p. 107).

the liver were made immediately after death, and the proportion of glycogenic matter, not sugar, was estimated. His results are, consequently, much more reliable and satisfactory. In a number of analyses of the livers of dogs confined to different articles of diet, Pavy found a little over seven per cent. of glycogenic matter, upon a diet of animal food; over seventeen per cent., upon a diet of vegetable food; and fourteen and a half per cent., upon a diet of animal food and sugar.[1] These results have been confirmed by M'Donnell, who, in addition, found that hardly a trace of amyloid substance could be detected in the liver on a diet of fat, and none whatever upon a diet of gelatine.[2] Bernard had already observed that the amount of sugar produced by the liver on a diet of fat was the same as during total abstinence from food.[3] These facts are entirely in accordance with observations upon the effects of different kinds of food in diabetes, and they have an important bearing upon the dietetic measures to be employed in this disease.

The effect of entire deprivation of food is to arrest the production of sugar in the liver, three or four days before death.[4] This arrest of the glycogenic function has generally been observed in cases of disease, except when death has occurred suddenly.

Influence of the Nervous System, etc.—Bernard has studied the influence of the nervous system upon the production of sugar more satisfactorily than any other of the variations of the glycogenic function, for the reason that he has noted these modifications by determining the sugar in the blood and the urine. Some of the points with regard to the nervous system we will consider again in another volume; and it is sufficient, in this connection, to mention the

[1] PAVY, *op. cit.*, p. 33, *et seq.*

[2] M'DONNELL, *Observations on the Functions of the Liver*, Dublin, 1865, p. 14.

[3] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 137.

[4] BERNARD, *op. cit.*, p. 129.

main results of some of the most striking of the experiments on this subject.

Fig. 13.

Instrument for puncturing the floor of the fourth ventricle (BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 290).

The most remarkable experiment upon the influence of the nervous system on the liver is the one in which artificial diabetes is produced by irritation of the floor of the fourth ventricle. This operation is not difficult, and is one that we have often repeated. The instrument used is a delicate stilet, with a flat cutting extremity, and a small projecting point, about $\frac{1}{25}$ of an inch long.[1] In performing the operation upon a rabbit, the head of the animal is firmly held in the left hand, and the skull is penetrated in the median line, just behind the superior occipital protuberance. This can easily be done by a few lateral movements of the instrument. Once within the cranium, the instrument is passed obliquely downward and forward, so as to cross an imaginary line between the two auditory canals, until its point reaches the basilar process of the occipital bone. The point then penetrates the medulla oblongata, between the roots of the auditory nerves and the pneumogastrics, and, by its projection, serves to protect the nervous centre from more serious injury from the cutting edge. The instrument is then carefully withdrawn, and the operation is completed.[2] This experiment is almost painless, and it is not desirable to administer an anæsthetic, as this, in itself, would disturb the glycogenic process. The urine may be drawn before the operation, by pressing the lower part of the abdomen, taking care not to

[1] These instruments have been made by Messrs. Tiemann & Co., of this city.

[2] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 291, *et seq.*

allow the bladder to pass up above the point of pressure, and it will be found turbid, alkaline, and without sugar. In one or two hours after the operation, the urine will have become clear, acid, and will react readily with any of the copper-tests. When this operation is performed without injuring the adjacent organs, the presence of sugar in the urine is only temporary, and the next day, the secretion

FIG. 14.

Section of the head of a rabbit, showing the operation of puncturing the floor of the fourth ventricle. *a*, cerebellum; *b*, origin of the seventh pair of nerves; *c*, spinal cord; *d*, origin of the pneumogastric; *e*, opening of entrance of the instrument into the cranium; *f*, instrument; *g*, fifth pair of nerves; *h*, auditory canal; *i*, extremity of the instrument on the spinal cord after having penetrated the cerebellum; *k*, occipital venous sinus; *l*, tubercula quadrigemina; *m*, cerebrum; *n*, section of the atlas. —(BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 298.)

will have returned to its normal condition. It is best, in performing this experiment, to operate on an animal in full digestion, when the production of sugar is at its maximum.

The production of diabetes in this way, in animals, is exceedingly interesting in its relations to certain cases of the disease in the human subject, in which the affection is traumatic, and directly attributable to injury near the medulla.

Its mechanism it is difficult to explain. The irritation is not propagated through the pneumogastric nerves, for the experiment succeeds after both of these nerves have been divided;[1] but the influence of the pneumogastrics upon glycogenesis is curious and interesting. If both of these nerves be divided in the neck, in a few hours or days, depending upon the length of time that the animal survives the operation, no sugar is to be found in the liver, and there is reason to believe that the glycogenic function is arrested. After division of the nerves in this situation, galvanization of their peripheral ends does not affect the production of sugar; but, by galvanization of the central ends, an impression is conveyed to the nervous centre, which is reflected to the liver, and produces a hypersecretion of sugar.[2] These questions will be referred to again, in connection with the physiology of the nervous system.

With regard to the influence of the sympathetic system upon the glycogenic function, there have been few experiments which lead to conclusions of any great value. Pavy found that division of the sympathetic filaments accompanying the vertebral arteries produced diabetes, but the operation was complicated by lesions of the vessels, which rendered the results somewhat unsatisfactory.[3]

It has been observed that the inhalation of anæsthetics and irritating vapors produces temporary diabetes;[4] and this has been attributed to the irritation conveyed by the pneumogastrics to the nerve-centre, and reflected, in the form of a stimulus, to the liver. It is for this reason that we should avoid the administration of anæsthetics in all accurate experiments on the glycogenic function. In illustration of this fact, Pavy has collected twenty cases, in which

[1] BERNARD, *loc. cit.*, p. 317.

[2] BERNARD, *op. cit.*, p. 324. It has been observed by Bernard that division of the pneumogastrics in the chest, between the lungs and the liver, does not affect the production of sugar (p. 328).

[3] PAVY, *op. cit.*, p. 87, *et seq.*

[4] BERNARD, *op. cit.*, p. 327.

chloroform was administered in the human subject for surgical operations, in all of which the passage of a small quantity of sugar in the urine was noted.[1]

Destination of Sugar.—Although sugar is constantly produced by the liver and taken up by the circulation, it is exceptional to find it in the blood after it has passed through the lungs. It is difficult to ascertain the precise mode of its destruction in the lungs, and, indeed, the nutritive function of sugar in the economy is not thoroughly understood. All that we can say of the destination of liver-sugar is, that it probably has the same office in nutrition as the sugar taken as food and that resulting from the digestion of amylaceous matters. The facts bearing upon this question will be reviewed under the head of nutrition.

Alleged Production of Fat by the Liver.—It is stated by Bernard, that in animals fed largely with saccharine and amylaceous principles, the blood of the hepatic veins contains an emulsive matter, which seems to be fat combined with a proteine substance. In support of the opinion that fat is thus produced in the liver, he brings forward that well-known fact, that a diet of starch and sugar is particularly favorable to the development of adipose tissue.[2] But the examinations of the matter supposed to be fatty have not been sufficiently minute to lead to any positive conclusions with regard to its character or composition. Rouget states, unreservedly, that this substance is simply glycogenic or amyloid matter.[3] While there can be no doubt of the formation of fat in the organism independently of the fat taken as food, there is not sufficient ground for regarding the liver as one of the organs specially concerned in its production.

[1] *Op. cit.*, p. 80.

[2] BERNARD, *Leçons de physiologie expérimentale*, Paris, 1855, p. 154.

[3] ROUGET, *Des substances amyloïdes.—Journal de la physiologie*, Paris, 1859, tome ii., p. 324.

Changes in the Albuminoid and the Corpuscular Elements of the Blood in passing through the Liver.—In verifying the observations of Bernard upon the presence of sugar in the blood of the hepatic veins, Lehmann was led to observe other differences in the composition of the blood from these vessels, as compared with the portal blood and the blood of the arterial system. One of the most important of these was the absence of fibrin. While the portal blood coagulates strongly, like blood from any other part of the body, the blood of the hepatic veins does not coagulate, and "the fibrin is either entirely absent, or is present in mere traces."[1] This observation has been confirmed by Brown-Séquard,[2] and, later, by M'Donnell, who describes a peculiar caseous matter as existing specially in the blood of the hepatic veins.[3] Lehmann also noted that the proportion of serum to corpuscles was much less in the hepatic than in the portal blood. The serum from the hepatic veins was found to present a diminution in albumen, amounting to fully one-third.

Some very curious observations were also made by Lehmann upon the blood-corpuscles in the hepatic vessels. He estimated that the proportion of white corpuscles in the blood of the hepatic veins was at least fivefold the proportion in the portal blood. He also noted certain differences in the appearance of the red corpuscles, which he explained by the supposition that the liver was the seat of development of these elements, which were formed from the white corpuscles, and that the blood of the hepatic veins contained a

[1] LEHMANN, *Physiological Chemistry*, Philadelphia, 1855, vol. i., p. 489. Several years before, Simon observed that fibrin was separated with difficulty from the blood of the hepatic veins, and was not to be found in the blood of the renal veins (SIMON, *Animal Chemistry*, Philadelphia, 1846, pp. 174, 178).

[2] BROWN-SÉQUARD, *Sur des faits qui semblent montrer que plusieurs kilogrammes de fibrine se forment et se transforment, chaque jour dans le corps de l'homme.*—*Journal de la physiologie*, Paris, 1858, tome i., p. 300.

[3] M'DONNELL, *Observations on the Functions of the Liver*, Dublin, 1865, p. 34.

greater number of "newly-formed or rejuvenescent blood-corpuscles."[1]

It is not our purpose, in this connection, to discuss the development of the corpuscular elements of the blood; but it is interesting to note the above-mentioned changes in the blood as it passes through the liver. The physiological significance of the destruction of fibrin and albumen is not understood, although the fact is undoubted.

[1] *Op. cit.*, pp. 498, 499.

CHAPTER XI.

THE DUCTLESS GLANDS.

Probable office of the ductless glands—Anatomy of the spleen—Fibrous structure of the spleen (trabeculæ)—Malpighian bodies—Spleen-pulp—Vessels and nerves of the spleen—Some points in the chemical constitution of the spleen—State of our knowledge concerning the functions of the spleen—Variations in the volume of the spleen during life—Extirpation of the spleen—Anatomy of the suprarenal capsules—Cortical substance—Medullary substance—Vessels and nerves—Chemical reactions of the suprarenal capsules—State of our knowledge concerning the functions of the suprarenal capsules—Extirpation of the suprarenal capsules—Addison's disease—Anatomy of the thyroid gland—State of our knowledge concerning the functions of the thyroid gland—Anatomy of the thymus—Pituitary body and pineal gland.

CERTAIN organs in the body, with a structure resembling, in some regards, the true glands, but without excretory ducts, have long been the subject of physiological speculation; and the most extravagant notions concerning their functions have prevailed in the early history of the science. The discovery of those functions of the liver which consist in modifications in the composition of the blood dimly indicated the probable office of the ductless glands; for, as far as the production of sugar is concerned, the liver belongs to this class. Indeed, the supposition that the ductless glands effect some change in the blood is now regarded by physiologists as the most reasonable of the many theories that have been entertained concerning their office in the economy; and this view is adopted by those, even, who do not admit the existence of a glycogenic function in the liver. Under

this idea, these organs have been called blood-glands, or vascular glands; but inasmuch as the supposition that these parts effect changes in the blood or lymph is merely to supply the want of any definite idea of their function, and rests mainly upon analogy with certain of the functions of the liver, we shall retain the name, ductless glands, as indicating the most striking of their anatomical peculiarities.

As far as presenting any definite and important physiological information is concerned, we might terminate here the history of the ductless glands. It is true that the largest of them, the spleen, has been extensively experimented upon by the earlier physiologists; but in point of fact, investigations have done little more than exhibit a want of knowledge of the functions of these remarkable organs; and the literature of the subject is mainly a collection of wild speculations and fruitless experiments. There are, however, some interesting experimental facts with relation to the spleen and the suprarenal capsules; though they are not very instructive, except that they indicate the extremely narrow limits of our positive knowledge. These few facts, with a sketch of the anatomy of the parts, will embrace all that we shall have to say concerning the ductless glands. Under this head are classed, the spleen, suprarenal capsules, thyroid gland, thymus, and sometimes the pituitary body and the pineal gland. These parts have certain anatomical points in common with each other, but on account of our want of knowledge of their functions, it is difficult to distinguish, as we have done in other organs, their physiological anatomy.

Anatomy of the Spleen.

The spleen is found, with but few exceptions, in all vertebrate animals, but does not exist in the invertebrata.[1] It

[1] This organ, according to Van der Hoeven, is not found in the cyclostomes and the lepidosiren (*Handbook of Zoology*, Cambridge, 1858, vol. ii., p. 29); and Milne-Edwards states that it is absent also in the amphioxus (*Leçons sur la*

is situated in the left hypochondriac region, next the cardiac extremity of the stomach. Its color is of a dark bluish-red, and its consistence is rather soft and friable. It is shaped somewhat like the tongue of a dog, presenting above, a rather thickened extremity, which is in relation with the diaphragm, and below, a pointed extremity, in relation with the transverse colon. Its external surface is convex, and its internal surface concave, presenting a vertical fissure, the hilum, giving passage to the vessels and nerves. It is connected with the stomach by the gastro-splenic omentum, and is still farther fixed by a fold of the peritoneum passing to the diaphragm. It is about five inches in length, three or four inches in breadth, and a little more than an inch in thickness. Its weight is between six and seven ounces. In the adult it attains its maximum of development, and diminishes slightly in size and weight in old age. In early life it bears about the same relation to the weight of the body as in the adult.[1] It is frequently hypertrophied to an enormous extent in disease, weighing sometimes as much as twenty pounds.[2]

The external coat of the spleen is the peritoneum; which is very closely adherent to the subjacent fibrous structure. The proper coat is dense and resisting; but in the human subject is quite thin and somewhat translucent. It is composed of inelastic fibrous tissue, mixed with numerous small fibres of elastic tissue and a few unstriped muscular fibres.

At the hilum the fibrous coat penetrates the substance of the spleen in the form of sheaths for the vessels and nerves; an arrangement entirely analogous to the fibrous

physiologie, Paris, 1862, tome vii., p. 235). According to Gray, the spleen exists without exception in all the vertebrate animals (*Structure and Use of the Spleen*, London, 1854, p. 272).

[1] Mr. Gray, in his elaborate essay on the spleen, gives a very extended table of the weight of this organ at different periods of life (*Structure and Use of the Spleen*, London, 1854, p. 76).

[2] Gray, *Anatomy, Descriptive and Surgical*, Philadelphia, 1862, p. 685.

sheath in the liver. The number of the sheaths in the spleen is equal to the number of arteries that penetrate the organ. This is sometimes called the capsule of Malpighi.[1] The fibrous sheaths are closely adherent to the surrounding substance, but are united to the vessels by a loose fibrous net-work. They follow the vessels in their ramifications to the smallest branches, and are lost in the spleen-pulp. Between the sheath and the outer coat, are numerous bands or trabeculæ of the same structure as the fibrous coat. The presence of elastic fibres in these structures can be easily demonstrated, and this kind of tissue is very abundant in the herbivora. In the carnivora the muscular tissue is particularly abundant, and can be readily demonstrated;[2] but in man this is not so easy, and the fibres are less numerous. There can be no doubt, however, that muscular tissue exists in the human subject throughout the whole extent of the fibrous structure, and the fibres are demonstrated without much difficulty in the trabeculæ.[3]

These peculiarities in the fibrous structure are important in their relation to certain physiological changes in the size of the spleen. Its contractility can be easily demonstrated in the dog by the application of a galvanic current to the nerves as they enter at the hilum. This is followed by a prompt and energetic contraction of the organ. Contractions may be produced, though they are much more feeble, by applying the current directly to the spleen.[4]

The substance of the spleen is soft and friable; and a portion of it, the spleen-pulp, may be easily pressed out, or even washed away by a current of water. Aside from the vessels and nerves, it presents for study: 1. An arrange-

[1] Malpighi, *De Liene, Opera Omnia*, Lugd. Batav., 1687, tomus ii., p. 294.

[2] Kölliker has demonstrated the presence of muscular fibres in considerable numbers in the dog, pig, ass, and cat; but they were not discovered in the rabbit, horse, ox, hedgehog, porpoise, or bat (*Handbuch der Gewebelehre*, Leipzig, 1867, S. 449).

[3] Sappey, *Traité d'anatomie*, Paris, 1857, tome iii., p. 323.

[4] Bernard, *Leçons sur les liquides de l'organisme*, Paris, 1859, tome ii., p. 421.

ment of fibrous bands, or trabeculæ, by which it is divided into innumerable communicating cellular interspaces. 2. Closed vesicles (Malpighian bodies), attached to the walls of the blood-vessels. 3. A soft, reddish substance, containing numerous cells and free nuclei, called the spleen-pulp.

Fibrous Structure of the Spleen (*Trabeculæ*).—From the internal face of the investing membrane of the spleen, and from the fibrous sheath of the vessels (capsule of Malpighi) are numerous bands, or trabeculæ, which, by their interlacement, divide the substance of the organ into irregularly-shaped, communicating cavities. These bands are from $\frac{1}{35}$ to $\frac{1}{15}$ of an inch broad, and are composed, like the proper coat, of ordinary fibrous tissue with elastic fibres and a few smooth muscular fibres. They pass off from the capsule of Malpighi and the fibrous coat at right angles, very soon branch, interlace, and unite with each other, becoming smaller and smaller, until they measure from $\frac{1}{250}$ to $\frac{1}{50}$ of an inch.[1] The smaller bands are cylindrical, and it is in these that the muscular tissue can be demonstrated with the greatest facility. As we should expect from the very variable size of the trabeculæ, the dimensions as well as the form of the cavities are exceedingly irregular. This fibrous net-work serves as a skeleton or a support for the softer and more delicate parts.

Malpighian Bodies.—In the very elaborate work on the spleen, by Malpighi, is a full account of the closed follicles, which have since been called the Malpighian bodies.[2] They are sometimes called the splenic corpuscles or glands. They are in the form of rounded or slightly-ovoid corpuscles, about $\frac{1}{75}$ of an inch in diameter, consisting of a delicate membrane, generally homogeneous, but sometimes faintly striated, with semifluid contents. In their form, size, and structure, they

[1] SAPPEY, *Traité d'anatomie*, Paris, 1857, tome iii., p. 323.

[2] MALPIGHI, *De Liene*, *Opera Omnia*, Lugd. Batav., 1687, tomus ii., p. 300.

bear a close resemblance to the closed follicles of the small intestine.[1] The investing membrane has no epithelial lining, and the contents consist of an albuminoid liquid, with numerous small, nucleated cells, and a few free nuclei. The cells measure from $\frac{1}{3000}$ to $\frac{1}{2500}$ of an inch in diameter. Both the cells and the free nuclei of the splenic corpuscles bear a close resemblance to cells and nuclei found in the spleen-pulp. The corpuscles are surrounded by blood-vessels, which send branches into the interior to form a delicate capillary plexus.[2]

The number of the Malpighian corpuscles in a spleen of ordinary size has been estimated by Sappey at from seven thousand to eight thousand.[3] They are readily made out in the ox and sheep, but are frequently not to be discovered in the human subject. In about forty examinations, in man, Sappey found them in only four; but in these they presented the same characters as in the ox and the sheep, and resisted decomposition for twelve days,[4] showing that it is not necessary to have recourse to perfectly fresh specimens to discover them if they exist. Kölliker notes the fact that they are often absent in the human subject when death has taken place from disease or long abstinence. He believes that they are nearly always to be found in perfectly healthy persons.[5] The occasional absence of these bodies constitutes another point of resemblance to the solitary glands of the small intestine.[6]

The relations of the Malpighian bodies to the arterial branches distributed through the spleen are peculiar. In specimens in which these corpuscles are easily made out, if a thin section be made, and the spleen-pulp be washed away by a stream of water, the corpuscles may be seen attached in some parts to the sides of the vessels, in others lying in

[1] See vol. ii., Digestion, p. 321.

[2] KÖLLIKER, *Handbuch der Gewebelehre*, Leipzig, 1867, S. 456.

[3] SAPPEY, *op. cit.*, p. 326.

[4] Idem., p. 325.

[5] KÖLLIKER, *op. cit.*, S. 454.

[6] See vol. ii., Digestion, p. 319.

ie notch formed by the branching of a vessel, and in others ttached to an extremity of an arterial twig, the vessel then reaking up into a plexus to surround the corpuscle. According to Sappey, the corpuscles are attached to arteries measuring from $\frac{1}{80}$ to $\frac{1}{60}$ of an inch or less in diameter.[1] When the artery is enclosed in its fibrous sheath, the corpuscles are applied to the sheath, but in the smallest arteries they are attached to the walls of the vessel. The attachment of the Malpighian bodies to the vessels is very firm, and they cannot be separated without laceration of the membrane.

Spleen-pulp.—With regard to the constitution of the spleen-pulp, there is considerable diversity of opinion. While anatomists and physiologists are pretty generally agreed concerning the structure and relations of the Malpighian bodies, some minutely describe cells in the pulp, the existence of which is denied by others of equal authority. The pulp, however, contains the essential elements of the spleen, and an accurate knowledge of all the structures contained in it could hardly fail to throw some light on its function; but there is so little that is definitely known of either the anatomy or the physiology of the spleen, that we shall refrain from discussing the views of different authors, referring the reader for full information upon these points to the elaborate works upon general anatomy.

The pulp is a dark, reddish, semifluid substance, its color varying in intensity in different specimens. It is so soft that it may be washed by a stream of water from a thin section, and it readily decomposes, becoming then nearly fluid. It is contained in the cavities bounded by the fibrous trabeculæ, and itself contains numerous microscopic bands of fibres arranged in the same way. It surrounds the Malpighian bodies, contains the terminal branches of the blood-vessels, and probably the nerves and lymphatics. Upon microscopi-

[1] *Op. cit.*, p. 328.

cal examination, it presents numerous free nuclei and cells, like those described in the Malpighian bodies; but the nuclei are here relatively much more abundant. In addition are found, blood-corpuscles, white and red, some natural in form and size, others more or less altered, with pigmentary granules, both free and enclosed in cells. Anatomists have attached a great deal of importance to large vesicles enclosing what have been supposed by some to be blood-corpuscles, and by others to be pigmentary corpuscles. The state of our knowledge on these points, however, is very unsatisfactory. Some authorities deny the existence of the so-called blood-corpuscle-containing cells. A writer in the *British and Foreign Medico-Chirurgical Review*, in 1853, after a thorough analysis of the various original observations that had appeared up to that time, came to the conclusion that the presence in the spleen-pulp of cells containing blood-corpuscles in a transition state was extremely doubtful;[1] and Kölliker, who has investigated the structure of the spleen with peculiar care, has advanced, in successive publications, several entirely different opinions on the subject.[2] We shall therefore abstain from a discussion of these disputed questions, which are at present of a character purely anatomical. All that we can say of the spleen-pulp is, that it contains cells, nuclei, blood-corpuscles, and pigmentary granules, with a yellowish-red fluid; and that it is intersected with microscopic trabeculæ of fibrous and muscular tissue, and a delicate net-work of blood-vessels. It is difficult to determine whether the blood-corpuscles come from vessels that have been divided in making the preparation, or are really free in the pulp; or whether the free nuclei are normal or come from cells that have been artificially ruptured.

[1] Wharton Jones, *British and Foreign Medico-Chirurgical Review*, London, 1853, vol. xi., p. 32.

[2] Kölliker, *Cyclopædia of Anatomy and Physiology*, London, 1847–1849, vol. iv., p. 771, Article, *Spleen*.

—— *Manual of Human Microscopic Anatomy*, London, 1860, p. 358, *et seq.*

—— *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 448, *et seq.*

Vessels and Nerves of the Spleen.—The quantity of blood which the spleen receives is very large in proportion to the size of the organ. The splenic artery is the largest branch of the cœliac axis. It is a vessel of considerable length, and is remarkable for its excessively tortuous course. In a man of between forty and fifty years of age, the vessel measured about five inches, without taking account of its deflections; and a thread placed on the vessel, so as to follow exactly all its windings, measured a little more than eight inches.[1] The large caliber of this vessel and its tortuous course are interesting points in connection with the great variations in size and situation which the spleen is liable to undergo in health and disease. The artery gives off several branches to the adjacent viscera in its course, and as it passes to the hilum divides into three or four branches, which again divide so as to form from six to ten vessels. These penetrate the substance of the spleen, with the veins, nerves, and lymphatics, enveloped in the fibrous sheath, the capsule of Malpighi. In the substance of the spleen the arteries branch rather peculiarly, giving off many small ramifications in their course, generally at right angles to the parent trunk. These are accompanied by the veins until they are reduced to from $\frac{1}{50}$ to $\frac{1}{60}$ of an inch in diameter. The two classes of vessels then separate, and the arteries have attached to them the corpuscles of Malpighi. It is also a noticeable fact that the distinct trunks passing in at the hilum have but few inosculations with each other in the substance of the spleen, so that the organ is divided up into from six to ten vascular compartments. This arrangement was observed many years ago by Assollant.[2]

The veins join the fine branches of the arteries in the spleen-pulp and pass out of the spleen in the same sheath. They anastomose quite freely in their larger as well as their

[1] SAPPEY, *Traité d'anatomie*, Paris, 1857, tome iii., p. 327.

[2] ASSOLLANT, *Recherches sur la rate.—Thèse*, No. 112, Paris, an xii. (1804), p. 36.

smaller branches. Their caliber is estimated by Sappey as about twice that of the arteries. This author regards the estimates, that have put the caliber of the veins at four or five times that of the arteries, as much exaggerated.[1] The number of veins emerging from the spleen is equal to the number of arteries of supply.

The lymphatics of the spleen are not numerous. By most anatomists, two sets of vessels have been recognized, the superficial and the deep; but those who have studied the subject practically have found it very difficult to demonstrate the superficial layer. Sappey denies the existence of any but the deep vessels;[2] and Kölliker admits that the superficial vessels are generally not to be found in morbid spleens, and are very scanty in perfectly healthy specimens.[3] The deep lymphatics have been demonstrated in the capsule of Malpighi, attached to the veins and emerging with them at the hilum. At the hilum, according to Kölliker, the deep vessels are joined by a few from the surface of the spleen. The vessels, numbering five or six, then pass into small lymphatic glands, and empty into the thoracic duct opposite the eleventh or twelfth dorsal vertebra. It was an old idea that the lymphatics were the excretory ducts of the spleen.[4] This view was revived by Hewson,[5] but it is a speculation which does not demand any discussion at the present day.

The nerves of the spleen are derived from the solar plexus. They follow the vessels in their distribution, and are enclosed with them in the capsule of Malpighi. They

[1] *Op. cit.*, p. 329.

[2] SAPPEY, *Traité d'anatomie*, Paris, 1857, tome iii., p. 331.

[3] KÖLLIKER, *Handbuch der Gewebelehre*, Leipzig, 1867, S. 460.

[4] In Milne-Edwards's elaborate work on physiology, now in course of publication, is an exhaustive bibliographical review of the early works on the anatomy and physiology of the spleen. The idea that the lymphatics were its excretory ducts was advanced by Eller, in 1716. (MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 233, *et seq.*)

[5] HEWSON, *Works, Sydenham Society Publication*, London, 1846, p. 271.

are distributed ultimately in the spleen-pulp, but nothing definite is known of their mode of termination. We have already referred to the fact that when these nerves are galvanized, the non-striated muscles in the substance of the spleen are thrown into contraction.

Some Points in the Chemical Constitution of the Spleen.—Very little has been learned with regard to the probable function of the spleen, from the numerous chemical analyses that have been made of its substance. It will therefore be out of place to discuss its chemical constitution very fully, and we shall only refer to certain principles, the existence of which, in the spleen-substance, may be considered as pretty well determined. In the first place, cholesterine has been found to exist in the spleen constantly and in considerable quantity, and the same may be said of uric acid. In addition, chemists have extracted from the substance of the spleen, hypoxanthine, leucine, tyrosine, a peculiar crystallizable substance called, by Scherer, lienine, crystals of hæmatoidine, lactic acid, acetic acid, butyric acid, inosite, amyloid matter, and some indefinite fatty principles.[1] It is difficult, however, to say how far some of these principles are formed by the processes employed for their extraction, or are due to morbid action; certainly, physiologists have thus far been unable to connect them with any definite views of the probable function of the spleen.

State of our Knowledge concerning the Functions of the Spleen.—The spleen is almost universal in vertebrate animals; it is an organ of considerable size, and is very abundantly supplied with vessels and nerves; it has a complex structure, unlike that of any of the true glands; its tissue presents a variety of proximate principles; but it has no excretory duct, and no opportunity is afforded for the study of its secretion, except as it may be taken up by the current

[1] Milne-Edwards, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 259.

of blood. It must be admitted, also, that up to the present time, no definite physiological ideas have followed the elaborate microscopical and chemical examinations of the spleen. There have been only two methods of inquiry, indeed, which have promised any such results: First, a comparison of the blood and lymph going into and coming from the spleen, and an examination of the variations in the volume of the organ during life; and second, a study of the phenomena which follow its extirpation in living animals. A review of the literature of the subject will show that we have gained but little positive information from either of these methods.

The condition of the question of the influence of the spleen upon the composition of the blood is well illustrated in the last edition of Longet's elaborate work on physiology.[1] This author quotes opinions of the highest authorities, based chiefly upon microscopical investigations, some in favor of the view that the blood-corpuscles are destroyed, and others arguing that they are formed in the spleen, while he himself offers no opinion upon the subject.

Still there are certain established points of difference between the blood of the splenic artery and of the splenic vein. There can be no doubt of the fact that the blood coming from the spleen contains a large excess of white corpuscles. Donné was the first to call attention to this fact,[2] and his observations have been confirmed by Gray,[3] and many others.[4] It can by no means be considered settled, however, that the function of the spleen is to form white blood-corpuscles. In pathology, although great increase in the leucocytes of the blood frequently attends hypertrophy

[1] LONGET, *Traité de physiologie*, Paris, 1869, p. 378.

[2] DONNÉ, *Cours de microscopie*, Paris, 1844, p. 99. Donné states that the blood taken from the splenic veins presents nothing remarkable; but on pressing out that contained in the tissue of the organ, the white corpuscles were very abundant, and were even more numerous than the red.

[3] GRAY, *The Structure and Use of the Spleen*, London, 1854, p. 150.

[4] MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1857, tome i., p. 352, and 1862, tome vii., p. 256.

of the spleen, this condition is also observed when the spleen is perfectly healthy.

Diminution in the proportion of red corpuscles in the blood in passing through the spleen, in a very marked degree, has been noted by Béclard,[1] Gray,[2] and others, and this gives color to the supposition that the spleen is an organ for the destruction of the blood-corpuscles; but we know nothing of the importance or significance of this process, and it is not shown that the corpuscles exist in undue quantity in animals after the spleen has been removed. We learn nothing more definite from the fact that blood of the splenic vein seems to contain an unusual quantity of pigmentary matter.[3] In connection with the marked diminution in the proportion of blood-corpuscles, both Béclard[4] and Gray[5] observed a marked increase in the fibrin and albumen in the blood of the splenic vein.

The significance of the facts just stated is so little understood, that it would seem hardly necessary even to mention them, except as an illustration of the small amount of definite information regarding the functions of the spleen that has resulted from an examination of the blood coming from this organ. We know nothing of any changes effected by the spleen in the constitution of the lymph.

Variations in the Volume of the Spleen during Life.—One of the theories with regard to the function of the spleen, which merits a certain amount of consideration, is that it serves as a diverticulum for the blood, when there is a tendency to congestion of the other abdominal viscera. The first attempt to formularize this idea and support it by experimental observations was made by Dobson, in 1830. He noted the fact that the spleen was much larger in dogs, from

[1] BÉCLARD, *Recherches expérimentales sur les fonctions de la rate et sur celles de la veine porte.—Archives générales de médecine*, Paris, 1848, 4me série, tome xviii., pp. 143, 442.

[2] GRAY, *op. cit.*, p. 156.

[3] Idem., p. 147.

[4] BÉCLARD, *loc. cit.*, p. 443.

[5] GRAY, *loc. cit.*, p. 152.

four to five hours after eating, than during the intervals of digestion; and he formally advanced the opinion that the spleen serves as a diverticulum for the blood during the period when there is a great afflux to the digestive organs, and that the extent of its enlargement is in direct ratio to the amount taken into the stomach.[1] Of the accuracy of these experiments there can be no doubt;[2] but the second series of observations, in which Dobson attempted to show that large quantities of food cannot be taken with impunity by animals after the spleen has been extirpated, have not been so satisfactorily verified. We have often removed the spleen from dogs, the operation being followed by complete recovery, and have never noted any thing unusual after feeding the animals very largely. In one observation, an animal from which the spleen had been removed six weeks before ate at one time a little more than four pounds of beef-heart, nearly one-fifth of his weight (the dog weighing twenty-two pounds), without suffering the slightest inconvenience.

Dobson certainly established the fact that the spleen is greatly enlarged in dogs, from four to five hours after feeding, that its enlargement is at its maximum at about the fifth hour, and that it gradually diminishes to its original size during the succeeding twelve hours; but it is not apparent how far this is important or essential to the proper perform-

[1] DOBSON, *Structure et fonctions de la rate.—Archives générales de médecine*, Paris, 1830, tome xxiv., p. 431, *et seq.* The experiments and conclusions of Dobson are here quoted in full from the original memoir. Gray, who gives in his work upon the spleen a very full *résumé* of the various theories with regar to the functions of the spleen, quotes (page 23) a Gulstonian lecture by Stukeley, in 1722, in which the same idea is advanced, though it seems to be pu forward merely as a theory, without any attempt at experimental proo Hodgkin revived this opinion in 1822, but without presenting any positive proof of its accuracy (HODGKIN, *On the Uses of the Spleen.—Edinburgh Medical and Surgical Journal*, 1822, vol. xviii., p. 90).

[2] The changes in the volume of the spleen have been observed by many physiologists. Bernard noted, in addition, that the blood of the splenic vein red during abstinence and dark during digestion (*Liquides de l'organisme*, Par 1859, tome ii., p. 420).

ance of the functions of digestion and absorption. Experiments have shown that animals may live, digest, and absorb alimentary principles perfectly well after the spleen has been removed, and this has even been observed in the human subject; and in view of these facts, it is impossible to assume that the presence of the spleen, as a diverticulum for the blood, is essential to the proper action of the other abdominal organs.

Extirpation of the Spleen.—There is one experimental fact that has presented itself in opposition to nearly every theory advanced with regard to the function of the spleen; which is, that the organ may be removed from a living animal, and yet all the functions of life go on apparently as before. The spleen is certainly not essential to life, nor, as far as we know, to any of the important general functions. It has been removed over and over again from dogs, cats, and even from the human subject, and its absence is attended with no constant and definite changes in the phenomena of life. If it act as a diverticulum, this function is not essential to the proper operation of the organs of digestion and absorption; and if its office be the destruction or the formation of the blood-corpuscles, the formation of leucocytes, fibrin, uric acid, cholesterine, or any excrementitious matter, there are other organs which may accomplish these functions. What renders this question even more obscure is the fact that we have no knowledge of any constant modifications in the size or the functions of other organs as a consequence of removal of the spleen.[1] This is not surprising, however, when we reflect that one kidney can accomplish the function of uri-

[1] Béclard mentions several authorities who have noted enlargement of the lymphatic glands throughout the system, consequent upon removal of the spleen, and one of these instances occurred in the human subject (*Traité élémentaire de physiologie humaine*, Paris, 1859, p. 443); but these observations have not been confirmed sufficiently to warrant the supposition that the spleen belongs to the lymphatic system, particularly as its connections with the blood-vessels are very extensive, and its lymphatics are rather scanty.

nary excretion after the other has been removed, and that the single organ remaining does not present enlargement of the Malpighian bodies and the convoluted tubes.[1]

There are certain phenomena that sometimes follow removal of the spleen from the lower animals, which are curious and interesting, even if they do not afford much positive information. Extirpation of this organ is an old and a very common experiment. In the works of Malpighi, published in 1687, we find an account of an experiment on a dog, in which the spleen was destroyed, and the operation was followed by no serious results.[2] Since then it has been removed so often, and the experiments have been so universally negative in their results, that it is hardly necessary to cite authorities on the subject. There are numerous instances, also, in which it has been in part or entirely removed from the human subject, which it is unnecessary to refer to in detail; but in nearly every case, when there was no diseased condition to complicate the observation, the result has been the same as in experiments on the inferior animals.[3]

One of the phenomena to which we desire to call attention is the modification of the appetite. Great voracity in animals, after removal of the spleen, was noted by the

[1] See page 170.

[2] MALPIGHI, *De Liene*, *Opera omnia*, Lugd. Batav., 1687, tomus ii., p. 302.

[3] In the *Union médicale*, Paris, 1867, 21me année, Nos. 141, 142, pp. 340, 373, a case of splenotomy followed by complete recovery is reported by M. Péan. In succeeding numbers of the same journal, M. Magdelain has collected reports of nine cases of splenotomy performed on account of wounds of the abdomen, and six cases in which the spleen had been in part or entirely removed on account of disease. In all the cases of injury, the patients recovered, presenting afterward no unusual symptoms; but of the six cases of disease of the spleen, four of the patients died (*L'union médicale*, Paris, 1867, Nos. 144, 146, pp. 405, 431). Other cases of removal of the spleen in the human subject are quoted in the *New York Medical Journal*, 1868, vol. vii., p. 258, *et seq.* In HALLER, *Elementa Physiologiæ*, Bernæ, 1764, p. 421, is a full historical account of the early experiments on removal of the spleen in the lower animals; and Prof. Dunglison (*Human Physiology*, Philadelphia, 1856, vol. i., p. 583, *et seq.*) gives an account of experiments on animals, and cites numerous instances of its removal or absence in the human subject.

earlier experimenters, and formed the basis of some of their extravagant theories. Boerhaave mentions this fact in his *Animal Economy;*[1] and Dumas advances it in support of a theory that the spleen takes up the superabundant portion of the gastric fluid.[2] Later experimenters have observed this change in the appetite, and have noted that digestion and assimilation do not appear to be disturbed, the animals becoming unusually fat. Prof. Dalton has also observed that the animals, particularly dogs, sometimes present a remarkable change in their disposition, becoming unnaturally ferocious and aggressive.[3] We have frequently observed these phenomena after removal of the spleen; and in the following experiment, performed in 1861, they were particularly marked:

The spleen was removed from a young dog weighing twenty-two pounds, by the ordinary method; viz., making an incision into the abdominal cavity in the linea alba, drawing out the spleen, and exsecting it after tying the vessels. Before the operation the dog presented nothing unusual, either in his appetite or disposition. The wound healed rapidly, and after recovery had taken place, the animal was fed moderately once a day. It was noticed, however, that the appetite was excessively voracious; and the dog became so irritable and ferocious that it was dangerous to approach him, and it became necessary to separate him from the other animals in the laboratory. He would eat refuse from the dissecting-room, the flesh of dogs, fæces, etc. On February 11, 1861, about six weeks after the operation, having been well fed twenty-four hours before, the dog was brought before the class at the New Orleans School of Medicine, and ate a little more than four pounds of beef-heart, nearly one fifth of his weight. This he digested perfectly well, and the appetite was the same on the following day.

[1] Boerhaave, *Actio Lienis, Œconomia Animalis*, London, 1761, p. 80.

[2] Dumas, *Principes de physiologie*, Paris, 1803, tome iv., p. 611.

[3] Dalton, *A Treatise on Human Physiology*, Philadelphia, 1867, p. 195.

This dog had a remarkably sleek and well-nourished appearance.

The above is a striking example of the change in the appetite and disposition of animals after extirpation of the spleen; but these results are by no means invariable. We have often removed the spleen from dogs, and kept the animals for months without observing any thing unusual; and, on the other hand, we have observed the change in disposition and the development of an unnatural appetite, in animals after removal of one kidney; these effects were also very well marked in an animal with biliary fistula, that lived for thirty-eight days. In the latter instance, the voracity could be explained by the disturbance in digestion and assimilation produced by shutting off the bile from the intestine; but these phenomena occurring after removal of one kidney, which appeared to have no effect upon the ordinary functions, are not so readily understood. We have observed both increase in the appetite and the development of extraordinary ferocity after extirpation of one kidney almost invariably, since our attention has been directed to this point; and in those experiments of which records were preserved, these effects were very marked. In one, a dog lived for nearly two years with one kidney, and was finally killed. The appetite was voracious and depraved. He would eat dogs' flesh greedily. In another, death took place in convulsions, forty-three days after removal of one kidney, the animal having apparently recovered from the operation. This dog was very ferocious, had an extraordinary appetite, and would eat fæces, putrid dogs' flesh, etc., which the other dogs in the laboratory would not touch. The other dog entirely recovered from the operation of removing one kidney, and presented the same phenomena.

In view of the above facts, it must be admitted that the removal of the spleen in the lower animals and the human subject has thus far demonstrated nothing, except that this part is not essential to the proper performance of the vital

functions. The voracity which occasionally follows the operation in animals is one of the phenomena, like the increase in the size of animals after castration, for which physiologists can offer no satisfactory explanation.

It is evident from the foregoing considerations that, notwithstanding the great amount of literature on the anatomy and functions of the spleen, physiologists have no definite knowledge of any important office performed by this organ. With this conclusion, we pass to a consideration of the other ductless glands, the physiology of which is, unfortunately, even more unsatisfactory.

Suprarenal Capsules.

The theories that have been advanced with regard to the function of the suprarenal capsules have not, as a rule, been based upon anatomical investigations, but have taken their origin from pathological observations and experiments on living animals. This fact detracts from the physiological interest attached to the structure of these bodies, and we shall consequently treat of their anatomy very briefly.

The suprarenal capsules, as their name implies, are situated above the kidneys. They are small, triangular, flattened bodies, placed behind the peritoneum, and capping the kidneys at the anterior portion of their superior ends. The left capsule is a little larger than the right, and is rather semilunar in form, the right being more nearly triangular. Their size and weight are very variable in different individuals. Of the different estimates given by anatomists, we may state, as an average, that each capsule weighs about one hundred grains. They are about an inch and a half in length, a little less in width, and a little less than one-fourth of an inch in thickness.

The weight of the capsules, in proportion to that of the kidneys, presents great variations at different periods of life; and they are so much larger in the fœtus than after birth, that some physiologists, in default of any reasonable theory

of their function in the adult, have assumed that their office is chiefly important in intra-uterine life. Meckel states that they are easily distinguished in the fœtus of two months; at the end of the third month, they are a little larger and heavier than the kidneys; they are equal in size to the kidneys (though a little lighter) at four months; and, at the beginning of the sixth month, are to the kidneys as two to five. In the fœtus at term, the proportion is as one to three, and in the adult as one to twenty-three.[1] It was asserted by some of the older writers, that the capsules are larger in the negro than in the white races, but Meckel states that although he had observed this in a negress, he saw nothing of it in dissecting a negro.[2] This observation did not have much significance at that time; but since it has been supposed that the suprarenal capsules have some function in connection with the formation of pigment, authors have quoted it as important.

The color of the capsules is whitish-yellow. They are completely covered by a thin fibrous coat, which penetrates their interior, in the form of trabeculæ. Upon section, they present a distinct cortical and medullary substance. The cortex is yellowish, from $\frac{1}{25}$ to $\frac{1}{12}$ of an inch in thickness, surrounding the capsule entirely, and constituting about two-thirds of its substance. The medullary substance is whitish, very vascular, and is remarkably prone to decomposition, so that it is desirable to study the anatomy of these bodies in specimens that are perfectly fresh.

Structure of the Suprarenal Capsules.—These bodies have been closely studied by Frey,[3] Ecker,[4] Kölliker,[5] Har-

[1] Meckel, *Manual of General, Descriptive, and Pathological Anatomy*, Philadelphia, 1832, vol. iii., p. 394.

[2] *Loc. cit.*

[3] Frey, *Cyclopædia of Anatomy and Physiology*, London, 1849–1852, vol. iv., part ii., p. 827, Article, *Supra-Renal Capsules.*

[4] Ecker, *Nebennieren*, in Wagner's *Handwörterbuch der Physiologie*, Braunschweig, 1853, Bd. iv., S. 128, *et seq.*

[5] Kölliker, *Manual of Human Microscopic Anatomy*, London, 1860, p. 421, *et seq.*, and *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 514, *et seq*

ley,[1] and many others. Recently, a very elaborate account of their minute anatomy has been given by M. Grandry.[2] The parts examined by M. Grandry were taken from an executed criminal, aged nineteen years, before they had undergone any alteration, and were placed immediately in chromic acid. We do not propose to discuss fully all the minute details or the mooted questions in the anatomy of these parts, for these have very little physiological interest; and we refer the reader to the authorities just cited for a more complete account of their histology. It is sufficient for us to know that they have no excretory duct, and that their structure resembles that of the other ductless glands.

Cortical Substance.—The cortical substance is divided into two layers. The external is pale-yellow, and is composed of closed vesicles, rounded or ovoid in form, containing an albuminoid fluid, cells, nuclei, and fatty globules. This layer is very thin. The greater part of the cortical substance is of a reddish-brown color, and is composed of closed tubes. On making thin sections through the cortical substance, previously hardened in chromic acid and rendered clear by means of glycerine, numerous rows of cells are seen, arranged with great regularity, and extending, apparently, from the investing membrane to the medullary substance. On studying these sections with a high magnifying-power, it is evident that the cells are enclosed in tubes measuring from $\frac{1}{1000}$ to $\frac{1}{325}$ of an inch in diameter. Harley is of the opinion that these tubes are not simply bounded by fibrous processes from the external coat, but are lined by a structureless membrane.[3] This view is confirmed by the more recent observations of M. Grandry, made upon perfectly fresh specimens from the human sub-

[1] HARLEY, *Histology of the Supra-Renal Capsules.—The Lancet*, London, 1858, vol. i., pp. 551, 576.

[2] GRANDRY, *Mémoire sur la structure de la capsule surrénale de l'homme et de quelques animaux.—Journal de l'anatomie et de la physiologie*, Paris, 1867, tome iv., pp. 225, 389.

[3] *Loc. cit.*

ject;[1] but it is probably the fact that the rows of cells are enclosed in tubes through a portion only of the cortical substance, the membrane being absent in the deeper layers. The cells are granular, with a distinct nucleus and nucleolus, and a variable number of oil-globules. They measure from $\frac{1}{1750}$ to $\frac{1}{1000}$ of an inch in diameter. Grandry describes three kinds of tubes in what he calls the second layer of the cortical substance; viz., tubes filled with a strongly-refracting mass of needle-shaped crystals, like crystals of fat; tubes filled with finely-granular, nucleated cells, containing no fat; and tubes filled with nucleated cells containing numerous fatty granulations.[2] Between the tubes of the cortical substance are bands of fibrous tissue, connected with the covering of the capsule.

Medullary Substance.—The medullary substance is much paler and more transparent than the cortex. In its centre are numerous openings, marking the passage of its venous sinuses. It is penetrated in every direction by excessively delicate bands of fibrous tissue, which enclose blood-vessels, nerves, and numerous elongated closed vesicles, containing cells, nuclei, and granular matter. These vesicles, $\frac{1}{80}$ of an inch long and about $\frac{1}{400}$ of an inch broad, have been demonstrated by Grandry in the ox and in the human subject. The cells in the human subject are from $\frac{1}{1700}$ to $\frac{1}{1200}$ of an inch in diameter. They are isolated with difficulty, and are very irregular in their form. The nuclei measure about $\frac{1}{2500}$ of an inch.[3] The medullary substance is peculiarly rich in vessels and nerves.

[1] GRANDRY, *op. cit.*, p. 392. M. Grandry makes three layers in the cortical substance; but these he found more distinct in the inferior animals than in man. The external layer is composed of one, two, or three rows of rounded or ovoid closed vesicles; the second layer is formed of tubes; and the third layer is composed of elements like those contained in the tubes, but not enclosed either in tubes or vesicles. This division into three zones had previously been made by Arnold (*Journal of Anatomy and Physiology*, London and Cambridge, 1867, vol. i., p. 147; from VIRCHOW'S *Archiv*, January, 1866).

[2] *Loc. cit.*

[3] *Op. cit.*, pp. 232, 398.

Vessels and Nerves.—The blood-vessels going to the suprarenal capsules are very numerous, and are derived from the aorta, the phrenic, the cœliac axis, and the renal artery. Sometimes as many as twenty distinct vessels penetrate the capsule. In the cortical substance the capillaries are arranged in elongated meshes, anastomosing freely, and surrounding the tubes, but never penetrating them. In the medullary substance the meshes are more rounded, and here the vessels form a very rich capillary plexus. Two large veins pass out, to empty, on the right side, into the vena cava, and on the left into the renal vein. Other smaller veins empty into the cava, the renal, and the phrenic veins.

The nerves are very numerous, and are derived from the semilunar ganglia, the renal plexus, the pneumogastric, and the phrenic. Kölliker mentions that he has counted, in the human subject, thirty-three nervous trunks entering the right suprarenal capsule.[1] According to Grandry, the nerves pass directly to the medullary substance, but here their mode of distribution is unknown. In the medullary matter, however, are two ganglia, characterized by nerve-cells of the ordinary form, and situated close to the central vein.[2]

Nothing whatever is known of the lymphatics of the suprarenal capsules, and the existence of these vessels, even, is doubtful.

Chemical Reactions of the Suprarenal Capsules.—A few years ago M. Vulpian discovered in the medullary portion of the suprarenal capsules a peculiar substance, soluble in water and in alcohol, which gave a greenish reaction with the salts of iron and a peculiar rose-tint on the addition of iodine. He could not determine the same reaction with extracts from any other parts.[3] Later, in conjunction with M.

[1] KÖLLIKER, *Handbuch der Gewebelehre*, Leipzig, 1867, S. 520.

[2] *Op. cit.*, p. 400.

[3] VULPIAN, *Note sur quelques réactions propres à la substance des corps surrénales.*—*Comptes rendus*, Paris, 1856, tome xliii., p. 663.

Cloez, he discovered hippuric and taurocholic acid in the capsules of some of the herbivora.[1] Other researches have been made into the chemistry of these bodies, but without results of any great physiological importance.

State of our Knowledge concerning the Functions of the Suprarenal Capsules.

In 1855, the late Dr. Addison, of Guy's Hospital, published a remarkable memoir on a peculiar disease which he had found connected with disorganization of the suprarenal capsules. This disease, sometimes called Addison's disease, is characterized by bronzing of the skin, and is accompanied by serious disorders in nutrition. It was supposed to be invariably fatal. The peculiar discoloration of the surface, attended with disorganization of the suprarenal capsules, led physiologists to suppose that, perhaps, these bodies had some function connected with the formation of pigment; and, following the publication of Dr. Addison's memoir, we find quite a number of experiments on animals, consisting chiefly in extirpation of the capsules. Before this time there had been no reasonable theory, even, of the probable function of these bodies. As our first ideas of the relations of the suprarenal capsules to the formation of pigment were derived from cases of disease, it may not be out of place to consider briefly whether there be any invariable and positive connection between structural change in these organs and the affection known under the name of bronzed skin.

In the memoir by Dr. Addison, are reported eleven cases of anæmia, accompanied with bronzing of the skin, terminating fatally, and found, after death, to be attended with extensive disorganization of the suprarenal capsules.[2] The

[1] CLOEZ ET VULPIAN, *Note sur l'existence des acides hippuriques et choléiques dans les corps surrénales des animaux herbivores.—Comptes rendus*, Paris, 1857, tome xlv., p. 340.

[2] ADDISON, *On the Constitutional and Local Effects of Disease of the Supra-Renal Capsules*, London, 1855.

reports of these cases attracted a great deal of attention among physiologists as well as pathologists. A year later, Prof. I. E. Taylor, of Bellevue Hospital, reported seven cases of bronzed skin, in two of which the diagnosis of disease of the suprarenal capsules was verified by post-mortem examination.[1] Attention now being directed to this peculiar condition of the system, accompanied with discoloration of the skin, numerous cases were reported, from time to time, but some of them did not fully carry out the views of Dr. Addison. In 1858, Dr. Harley, in connection with his elaborate researches into the anatomy and physiology of the suprarenal capsules, cited several cases of the so-called Addison's disease, unaccompanied with any disorganization of the capsules, and also several instances in which the capsules were seriously invaded by disease, without any bronzing of the skin.[2] Perhaps the most extensive collection of cases, however, taken from a great number of authorities, is given by Dr. Greenhow, in a recent work on Addison's disease. Dr. Greenhow is apparently convinced that the connection between the constitutional symptoms and discoloration of the skin, described by Addison, and disorganization of the suprarenal capsules is well established. He reports one hundred and ninety-six cases; and, out of these, he selects one hundred and twenty-eight, as fair representatives of Addison's disease.[3] There are several cases (ten) in which there was bronzing of the skin, the suprarenal capsules being perfectly healthy; but in only one of these were there any of the

[1] TAYLOR, *The Sunburnt Appearance of the Skin as an early Diagnostic Symptom of Supra-Renal Capsule Disease.*—Reprinted from the *New York Journal of Medicine*, 1856.

[2] HARLEY, *An Experimental Inquiry into the Functions of the Supra-Renal Capsules, and their Supposed Connexion with Bronzed Skin.—British and Foreign Medico-Chirurgical Review*, London, 1858, vol. xxi., pp. 204, 498. Shortly after these papers appeared, we made an editorial analysis of them, in connection with the recent observations of MM. Brown-Séquard, Martin-Magron, Gratiolet, and Philipeaux, in the *Buffalo Medical Journal* (see vol. xiii., 1858, p. 575, and vol. xiv., p. 175).

[3] GREENHOW, *On Addison's Disease*, London, 1866, p. 47, *et seq.*

characteristic constitutional symptoms.[1] There are twenty-two cases cited of cancer of the suprarenal capsules, not one of which presented the characteristic constitutional symptoms, seven only presenting some slight discoloration of the skin.[2]

Without discussing this subject more fully, it seems justifiable to adopt the opinion, entertained by many pathologists, that there is a connection between bronzed skin accompanied with certain grave constitutional symptoms, and disorganization of the suprarenal capsules, which is frequent but not invariable; but it is not established that the destruction of the capsules stands in a causative relation to the discoloration or to the constitutional disturbance. It is more interesting to us, however, to know that the investigations into these diseased conditions have developed little or nothing of importance concerning the physiology of the suprarenal capsules.

Extirpation of the Suprarenal Capsules.—There are two important questions to be settled by the removal of the suprarenal capsules from living animals. The first is, whether or not these organs are essential to life; and the second is, to determine the consequences of their removal, as exhibited in modifications of the animal functions. The first experiments on this subject, by Dr. Brown-Séquard, seemed to show, not only that the suprarenal capsules are essential to life, but that they have an important function connected with the development of pigment. These experiments were in a measure complementary to the pathological observations by Dr. Addison.

Are the suprarenal capsules essential to life? This question can be answered in a very few words. Dr. Brown-Séquard,[3] in his first experiments, removed one and both

[1] *Op. cit.*, p. 49. [2] *Op. cit.*, p. 50.

[3] Brown-Séquard, *Recherches expérimentales sur la physiologie et la pathologie des corps surrénales.—Archives générales de médecine*, Paris, 1856, 5me série, tome viii., pp. 385, 572.

capsules in rabbits, Guinea-pigs, dogs, and cats, and the animals died in the course of two or three days. He also noted several peculiar results, as turning, and contraction of the pupil, when one capsule had been extirpated, and the development of peculiar crystals in the blood. M. Gratiolet repeated these experiments, and ascertained that the left capsule could be removed with impunity, while extirpation of the right was always fatal.[1] M. Philipeaux added a number of observations, experimenting chiefly on rats and taking great care to disturb the adjacent organs as little as possible. As the result of these experiments, he concluded that the capsules were not essential to life. Of four rats operated upon in this way, three died, as Philipeaux supposed, of cold, the first in nine days, the second in twenty-three days, and the third in thirty-four days. One was alive and well when the report was made, although the capsules had been removed for forty-nine days.[2] The views first advanced by Dr. Brown-Séquard were reiterated by him in a memoir published in the *Journal de la physiologie*, in 1858, with the modification that the capsules might have no important functions in animals without pigment, as white rabbits and rats, but that they were indispensable to the life of animals not albinos.[3] These views, however, were farther disproved by Dr. Harley, who made experiments upon a variety of animals, albinos and colored, with the most satisfactory results. Two Guinea-pigs were experimented upon by Dr. Harley, in the following way: In one the abdomen was opened, and the amount of injury which the parts would suffer by removal of the suprarenal capsules was inflicted, the wound was closed, and the capsules allowed to remain; and the other, of the same age, sex, and development, was

[1] GRATIOLET, *Note sur les effets qui suivent l'ablation des capsules surrénales.—Comptes rendus*, Paris, 1856, tome xliii., p. 469.

[2] PHILIPEAUX, *Note sur l'extirpation des capsules surrénales chez les rats albinos.—Comptes rendus*, Paris, 1856, tome xliii., p. 904.

[3] BROWN-SÉQUARD, *Nouvelles recherches sur l'importance des fonctions des capsules surrénales.—Journal de la physiologie*, Paris, 1858, tome i., p. 160, *et seq.*

deprived of the capsule on the corresponding side. Both animals died within twenty-four hours. Dr. Harley, among other experiments, took out both capsules from a piebald rat. The left was removed six weeks after the right. The animal entirely recovered and became fat and healthy looking.[1]

In such a question as this, negative experiments are of little account; and the instances in which animals have recovered and lived perfectly well after removal of both suprarenal capsules show conclusively that they are not essential to life. Death has probably been due, in most of the experiments, to injury of the semilunar ganglia, as suggested by Dr. Harley, and it is probably on account of the greater injury, from the situation of the capsule, produced by operating on the right side, that the removal of the capsule on that side is more generally fatal.

It is not necessary to take account, in this connection, of the contraction of the pupil, "turning" and other symptoms referable to the nervous system, which have sometimes followed these operations. These phenomena are undoubtedly due to injury of adjacent parts, and not to extirpation of the capsules. The only remaining question to determine is whether the capsules have any thing to do with the formation or change of pigment. Notwithstanding the assertion of Dr. Brown-Séquard, that flakes of pigment and blood-crystals differing from those found in normal blood are found in animals deprived of the suprarenal capsules, this view is adopted by few physiological authorities. Longet cites the observations of Martin-Magron,[2] who examined daily, with the greatest care, the blood of a cat that lived two months after extirpation of the capsules, and could never determine the pigmentary matters described by Brown-

[1] HARLEY, *An Experimental Inquiry into the Functions of the Supra-Renal Capsules, and their Supposed Connexion with Bronzed Skin.—British and Foreign Medico-Chirurgical Review*, London, 1858, vol. xxi., p. 204, *et seq.*

[2] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 392. It does not appear from this quotation that the experiments of Martin-Magron were ever published elsewhere.

Séquard. Dr. Harley, also, in one of the experiments in which the animal died, failed to find pigmentary matter.[1]

In view of these facts, and in the absence of comparative examinations of the blood going to the suprarenal capsules by the arteries and returned from them by the veins, it is impossible to assign any definite function to these bodies, and it is certain that they are not essential to life. Their greater relative size before birth has led to the supposition that they might have an important office in intra-uterine life, but this is a pure hypothesis, based upon no positive knowledge.

Thyroid Gland.

The history of this gland belongs almost exclusively to descriptive anatomy; and its only physiological interest is in the similarity of its structure to that of the other ductless glands. It has no excretory duct. It is attached to the lower part of the larynx, following it in its various movements. Its color is brownish-red. The anterior face is convex, and is covered by certain of the muscles of the neck. The posterior surface is concave, and is applied to the larynx and trachea. It is formed of two lateral lobes, with a rounded, thickened base below, and a long, pointed extremity extending upward, connected by an isthmus. Each of these lobes is about two inches in length, three-quarters of an inch in breadth, and about the same in thickness at its thickest portion. The isthmus connects the lower portion of the lateral lobes. It covers the second and third tracheal rings, and is about half an inch wide and one-third of an inch thick. From the left side of the isthmus, and sometimes from the left lobe, is a portion projecting upward, called the pyramid. The weight of the thyroid gland, according to Sappey, is from three hundred and fifty to three hundred and eighty grains. It is usually stated by anatomical writers that it is relatively

[1] *Loc. cit.*

larger in the fœtus and in early life, than in the adult; but Sappey, from his own researches, is disposed to believe that its weight, in proportion to the weight of the adjacent organs, does not vary with age.[1] It is a little larger and more prominent in the female than in the male.

Structure of the Thyroid Gland.—The gland is covered with a thin but resisting coat of ordinary fibrous tissue, which is loosely connected with the surrounding parts. From the internal surface of this membrane are numerous fibrous bands, or trabeculæ, giving off, as they pass through the gland, secondary trabeculæ, and then subdividing, until they become microscopic. By this arrangement, the gland is divided up into communicating cells, like a sponge. These bands are mingled with numerous small elastic fibres. Throughout the substance of the gland, lodged in the meshes of the trabeculæ, are numerous rounded or ovoid closed vesicles, measuring from $\frac{1}{500}$ to $\frac{1}{250}$ of an inch. These are formed of a structureless membrane, and lined by a single layer of pale, granular, nucleated cells, from $\frac{1}{3000}$ to $\frac{1}{2000}$ of an inch in diameter.[2] The layer of cells sometimes lines the vesicle completely, sometimes it is incomplete, and sometimes it is wanting. The contents of the vesicles are a clear, yellowish, slightly viscid, albuminoid fluid, with a few granules, pale cells, and nuclei. Robin has described in these vesicles some curiously-shaped, translucent, feebly-refracting, colorless bodies which he has called sympexions; but little is known of their constitution or properties.[3] The vesicles are arranged in little collections or lobes, with the great veins passing between them.

Vessels and Nerves.—The blood-vessels of the thyroid gland are very numerous, it being supplied by the superior

[1] Sappey, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 447.

[2] Kölliker, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 481.

[3] Littré et Robin, *Dictionnaire de médecine*, Paris, 1855, Articles, *Sympexion* and *Thyréoide*.

and inferior thyroid arteries, and sometimes a branch of the innominata. The arteries break up into a close capillary plexus, surrounding the vesicles with a rich net-work, but never penetrating their interior. The veins are large, and, like the hepatic veins, are so closely adherent to the surrounding tissue, that they do not collapse when cut across. The veins emerging from the gland form a plexus over its surface and the surface of the trachea, and then go to form the superior, middle, and inferior thyroid veins. The nerves are derived from the pneumogastric and the cervical sympathetic ganglia. The lymphatics are numerous, but are difficult to inject. The exact distribution of the nerves and the origin of the lymphatics are not well understood.

State of our Knowledge concerning the Functions of the Thyroid Gland.—It is generally admitted that the thyroid gland may be removed from animals without interfering with any of the vital functions; and this, taken in connection with the fact that it is so often diseased in the human subject, without producing any general disturbance, shows that its function cannot be very important. Nothing of importance has been learned from a chemical analysis of its substance. The blood of the thyroid veins has been analyzed by Colin and Berthelot, but the changes in its composition in passing through the gland are slight and indefinite.[1] An instance is quoted by Longet of periodical enlargement of the gland in a female during menstruation,[2] but there is no evidence that this is of constant occurrence.

Thymus Gland.

The anatomy of the thymus assimilates it to the ductless glands, but its function, whatever it may be, is confined to early life. In the adult the organ is wanting, traces, only, of fibrous tissue, with a little fat, existing after puberty in

[1] COLIN, *Traité de physiologie comparée*, Paris, 1856, tome ii., p. 479.
[2] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 398.

the situation previously occupied by this gland. As there never has been a plausible theory, even, of the function of this organ, the existence of which is confined to the first two or three years of life, we shall abstain from all discussions with regard to minute points in its anatomy, and give a simple sketch of its structure, as compared with the ductless glands already considered.

The thymus appears about the third month of fœtal life, and gradually increases in size until about the end of the second year. It then undergoes atrophy, and disappears almost entirely at the age of puberty. It is situated partly in the thorax and partly in the neck. The thoracic portion is in the anterior mediastinum, resting upon the pericardium, extending as low as the fourth costal cartilage. The cervical portion extends upward as far as the lower border of the thyroid. The whole gland is about two inches in length, one and a half inches broad at its lower portion, and about one-quarter of an inch thick. Its color is grayish, with a slightly rosy tint. It is usually in the form of two lateral lobes, lying in apposition in the median line, though sometimes there exists but a single lobe. It is composed of numerous lobules, held together by fibrous tissue.

The proper coat of the thymus is a delicate fibrous membrane, sending processes into the interior of the organ. Its fibrous structure, however, is loose, so that the lobules can be separated with little difficulty. Portions of the gland may be, as it were, unravelled, by loosening the interstitial fibrous tissue. In this way it will be found to be composed of numerous little lobular masses, attached to a continuous cord. This arrangement is more distinct in the inferior animals of large size than in man. The lobules are composed of rounded vesicles, from ten to fifteen in number, and from $\frac{1}{125}$ to $\frac{1}{40}$ of an inch in diameter. The walls of these vesicles are thin, finely granular, and excessively fragile. The vesicles contain a small quantity of an albuminoid fluid, with cells and free nuclei. The cells are small and transparent,

and the nuclei, spherical, relatively large, and containing from one to three nucleoli. The free nuclei are also rounded and contain several distinct nucleoli. These vesicles are easily ruptured, when their contents exude in the form of an opalescent fluid, sometimes called the thymic juice.

Anatomists are somewhat divided in their opinions with regard to the structure of the central cord and lobules. Some adopt the view advanced by Sir Astley Cooper,[1] that the cord has a central canal, connected with cavities in the lobules;[2] while others believe that the cavities thus described are produced artificially, by the processes employed in anatomical investigation.[3] The latter opinion is the latest, and is probably correct.

The blood-vessels of the thymus are numerous, but their caliber is small, and the gland is not very vascular. They are derived chiefly from the internal mammary artery, a few coming from the inferior thyroid, the superior diaphragmatic, or the pericardial. They pass between the lobules, surround and penetrate the vesicles, and form a capillary plexus in their interior. The vesicles, in this respect, bear a certain resemblance to the closed follicles of the intestine. The veins are also numerous, but they do not follow the course of the arteries. The principal vein emerges at about the centre of the gland, posteriorly, and empties into the left brachiocephalic. Other small veins empty into the internal mammary, the superior diaphragmatic, and the pericardial. A few nervous filaments from the sympathetic system surround the principal thymic artery, and penetrate the gland. Their ultimate distribution is uncertain. The lymphatics are very numerous.[4]

Inasmuch as the thymus is peculiar to early life, one of

[1] COOPER, *Anatomy of the Thymus Gland*, London, 1832, p. 26, *et seq.*

[2] *Cyclopædia of Anatomy and Physiology*, London, 1849–1852, vol. iv., Part ii., p. 1087, Article, *Thymus.*

[3] SAPPEY, *Traité d'anatomie descriptive*, Paris, 1857, tome iii., p. 456, and LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Thymus.*

[4] KÖLLIKER, *Handbuch der Gewebelehre des Menschen*, Leipzig, 1867, S. 485.

the most interesting points in its anatomical history relates to its mode of development. This, however, does not present any great physiological importance, and is fully treated of in works upon anatomy.[1]

Pituitary Body and Pineal Gland.

These little bodies, situated at the base of the brain, are quite vascular, contain closed vesicles and but few nervous elements, and are sometimes classed with the ductless glands. Physiologists have no idea of their function.

The pituitary body is of an ovoid form, a reddish-gray color, weighs from five to ten grains, and is situated in the sella turcica of the sphenoid bone. It is said to be larger in the fœtus than in the adult, and at that time has a cavity communicating with the third ventricle.[2] Ecker describes it as containing the elements of a blood-gland.[3] This little body has lately been studied by M. Grandry, in connection with the suprarenal capsules. He regards it as essentially composed of closed vesicles, with fibres of connective tissue and blood-vessels. The vesicles measure from $\frac{1}{315}$ to $\frac{1}{125}$ of an inch in diameter. They are formed of a transparent membrane, containing irregularly-polygonal, nucleated cells, and free nuclei. The cells are from $\frac{1}{2500}$ to $\frac{1}{1100}$ of an inch in diameter. The nuclei are distinct, with a well-marked nucleolus, and measure about $\frac{1}{5000}$ of an inch. Capillary vessels surround these vesicles, without penetrating them. M. Grandry did not observe either nerve-cells or fibres between the vesicles.[4] In old subjects he found the peculiar concre-

[1] For the history of the development of the thymus, the reader is referred to special treatises. A very full account of its development is given by Dr. Handfield Jones, in the *Cyclopædia of Anatomy and Physiology*, London, 1849–1852, vol. iv., Part ii., p. 1087, *et seq.*

[2] Gray, *Anatomy, Descriptive and Surgical*, Philadelphia, 1862, p. 519.

[3] Ecker, in Wagner, *Handwörterbuch der Physiologie*, Braunschweig, 1853, Bd. iv., S. 161.

[4] Grandry, *Glande pituitaire.—Journal de l'anatomie*, Paris, 1867, tome iv., p. 400, *et seq.*

tions (sympexions) already described as existing in the thyroid.[1]

The pineal gland is situated just behind the posterior commissure of the brain, between the nates, and is enclosed in the velum interpositum. It is of a conical shape, one-third of an inch in length, and of nearly the color of the pituitary body. It is connected with the base of the brain by several delicate commissural peduncles. It presents a small cavity at its base, and frequently contains in its substance little calcareous masses, composed of phosphate and carbonate of lime, phosphate of magnesia and ammonia, and a small quantity of organic matter.[2] It is covered with a fibrous envelope, which sends processes into its interior. As the result of the researches of M. Grandry, it has been found to present a cortical substance, entirely analogous in its structure to the pituitary body, and a central portion, composed of the ordinary nervous elements found in the gray matter of the brain. Its structure is regarded by Grandry as very like that of the medullary portion of the suprarenal capsules.[3]

It is difficult to classify organs, of the function of which we are entirely ignorant; but the structure of the little bodies just described certainly resembles that of the ductless glands. We have only indicated their anatomy to show that their function is probably analogous to that of the other organs of the same class.

[1] See page 360. [2] GRAY, *op. cit.*, p. 528.

[3] GRANDRY, *Glande pinéale.—Journal de l'anatomie*, Paris, 1867, tome iv., p. 405, *et seq.*

CHAPTER XII.

NUTRITION.

Nature of the forces involved in nutrition—Protoplasm—Definition of vital properties—Life, as represented in development and nutrition—Principles which pass through the organism—Principles consumed in the organism—Nitrogenized principles—Development of power and endurance by exercise (Training)—Non-nitrogenized principles—Formation and deposition of fat—Conditions under which fat exists in the organism—Physiological anatomy of adipose tissue—Conditions which influence nutrition—Products of disassimilation.

NUTRITION proper, in the light in which we propose to consider it in this chapter, is the process by which the physiological decay of the tissues and fluids of the body is compensated by the appropriation of new matter. All of the physiological processes that we have thus far studied, including circulation, respiration, alimentation, digestion, absorption, and secretion, are to be viewed in the light of means directed to a single end; and the great function, to which all the others are subservient, is the general process of nutrition.

The nature of the main forces involved in nutrition, be it in a highly-organized part, like the brain or muscles, or a tissue called extra-vascular, like the cartilages or nails, is unknown. The phenomena attending the general process, however, have been studied most carefully, and certain important positive results have been attained; but we find no more satisfactory explanation of the nature of the causative force of nutrition in the doctrines of to-day than in the speculative theories of Pythagoras.

We can hardly realize the vast extent of the problem of nutrition from a review of the functions which we have already considered. We have seen that the blood contains all the elements that enter into the composition of the tissues and secretions, either identical with them in form and composition, as is the case with the inorganic principles, or in a condition which allows of their transformation into the characteristic principles of the tissues, as we see in the organic substances proper. These materials are supplied to the tissues, in the required quantity, through the circulatory apparatus; and the oxygen, which is immediately indispensable to all the operations of life, is introduced by respiration. The great nutritive fluid, being constantly drawn upon by the tissues for materials for their regeneration, is kept at the proper standard by the introduction of new matter into the system, in alimentation, its elaborate preparation by digestion, and its appropriation by the fluids by absorption. These processes, many of them, require the action of certain secretions. The introduction of new matter, so essential to the continuance of the phenomena of life, is demanded, on account of the change of the substance of the tissues into what we call effete matter; and this is discharged from the animal organism, to be appropriated by vegetables, and thus maintain the equilibrium between these two great kingdoms in Nature.

What is it that causes the parts of a living animal organism to undergo change into effete matter, incapable of any further animal functions; and what is it that gives to these parts the power of self-regeneration, when new matter is presented under proper conditions?

These questions are the physiological *ignis fatuus*, which, it is to be feared, will forever elude the grasp of scientific inquiry. They constitute one of the great mysteries ever present in the minds of the student of Nature, and one, the grandeur of which is so immense that it is a problem with which our intelligence can scarcely grapple. Its greatness is com-

mensurate with that of the question of the soul, and its relations to the finite and the infinite; a question which philosophers have been constrained either to admit upon the faith of revelation, or to hopelessly abandon. Little, if any, real progress is to be made by endeavoring to cover the inscrutable problem of life with a simplicity entirely artificial. This will always be attractive, and, to a certain extent, satisfactory to the minds of those unacquainted with the details of natural laws, or willing to admit speculative theories upon subjects concerning which it is impossible, in the present condition of science, to have any positive information; and, if generally admitted by biological students, would carry our science back to the dark periods in its history, when the study of Nature was confined to speculation, and there existed no knowledge based upon the direct observation of phenomena. A new name, arbitrarily applied to organic matter, without any addition to its physiological history, does not advance our definite knowledge. For example, it has long been known that certain nitrogenized constituents of the organism, classed collectively as organic principles, seem to give to the tissues their property of self-regeneration and development. It may seem to those not engaged in scientific inquiry that a recital of the wonderful properties of "protoplasm" affords some additional information concerning the phenomena observed in organized bodies; but the true definition of the term leads us back to our former ideas of the so-called vital properties of organic matters.[1]

It is a well-established fact that while nearly all of the tissues undergo disassimilation, or conversion into effete matter, during their physiological decay in the living organism, others, like the epidermis and its appendages, are

[1] HUXLEY, *The Physical Basis of Life*, New Haven, 1869,—from the *Fortnightly Review*, for February, 1869. This very interesting and able discourse, delivered originally before a popular audience, is referred to, not as a subject for rigid scientific criticism, but as formularizing some of the prevalent ideas concerning the properties of the so-called protoplasm.

gradually desquamated, and, when once formed, do not pass through any further changes. An attempt has been made by Dr. Beale to distinguish in all the tissues a matter endowed with the so-called vital properties, which he calls germinal matter, and a "formed material," which is passive and cannot become the seat of vital actions.[1] Under this idea, the functions of nutrition and development are performed exclusively by germinal matter. This theory has been adopted by few physiologists; and we cannot but regard such a division as purely anatomical and artificial, as far as the physiology of nutrition is concerned. It is hardly more than a new statement of the old idea of the activity of the nucleus in the process of cell-development. We are not called upon to enter into an extended discussion of this question, until some facts are brought forward which would render such an hypothesis probable.

The whole question of the essence and nature of the nutritive property or force resolves itself into vitality. Life is always attended with what we know as the phenomena of nutrition, and nutrition does not exist except in living organisms. When we can state positively what is life, we shall know something of nutrition. At present, physiologists have only been able to define life by a recital of certain of its invariable and characteristic attendant conditions; and yet there are few, if any, definitions of life—regarding it as the sum of the phenomena peculiar to living organisms—that are not open to grave objections.

If we regard life as a principle, it stands in the relation of a cause to the vital phenomena; if we regard it as the totality of these phenomena, it is an effect.

If we study the development of a fecundated ovum, life seems to be a principle, giving the wonderful property of appropriating matter from without, until the germ becomes changed, from a globule of microscopic size and an

[1] TODD, BOWMAN, AND BEALE, *The Physiological Anatomy and Physiology of Man*, London, 1866, p. 87.

apparently simple structure, into a complete organism, with highly-elaborated parts. This organism has a definite form and size, a definite period of existence, and produces, at a certain time, generative elements, capable of perpetuating its life in new beings. We may say that an organism dies physiologically because the vital principle, if we admit the existence of a principle, has a limited term of existence. But, on the other hand, the fully-developed living organism, which we call an animal, presents numerous distinct parts, each endowed with an independent property called vital, that property recognized by Haller in various tissues, under the name of irritability; and it is the coördinated sum of these vitalities that constitutes the perfect being. These are more or less distinct; and we do not commonly observe a sudden and simultaneous arrest of the vital properties in all the tissues, in what we call death. For example, the nerves may die before the muscles, or the muscles, before the nerves. It is also found that vital properties, apparently lost or destroyed, may be made to return; as in resuscitation after asphyxia, or the restoration of muscular or nervous irritability by injection of blood.

The life of a fecundated ovum is the property which enables it to undergo a certain development when placed under favorable conditions; and, by the surrounding conditions, its development may be arrested, suspended, or modified. The life of a non-fecundated ovum is like that of any ordinary anatomical element.

The life of an anatomical element or tissue in process of development is the property by virtue of which it arrives at its perfection of organization, and performs certain defined functions, as far as its organization will permit. This can also be destroyed, suspended, or modified by surrounding conditions.

The life of a perfect anatomical element or tissue is the property which enables it to regenerate itself and perform its functions, subject, also, to modifications from surrounding conditions.

The life of a perfect animal organism is the sum of the vitalities of its constituent parts; but a being may live with the vitality of certain parts abolished or seriously modified, as a man exists and preserves his identity with a limb amputated. Life may continue for a long time without consciousness, or with organs paralyzed or their function destroyed; but certain functions, such as respiration or circulation, are indispensable to the nutrition of all parts, and the vitality of the different tissues is speedily lost when these processes are arrested, and the being then ceases to exist.

These considerations make it evident that it is difficult, if not impossible, to give a single comprehensive definition of life, a study of the varied phenomena of which constitutes the science of physiology.

The general process of nutrition begins with the introduction of matter from without, called food. It is carried on by the appropriation of this matter by the organism. It is attended with the production of excrementitious principles, and the development of certain phenomena that we have not yet studied, the most important of which is the production of heat. We shall have little to say about food, beyond what we have already considered under the head of alimentation, except to classify the alimentary principles with reference to their relations to the general process of nutrition.

Principles which pass through the Organism.

All of the inorganic principles taken in with the food pass out of the organism, generally in the form in which they enter, in the fæces, urine, and perspiration; but it must not be inferred from this fact that they are not useful as constituent parts of the body. Some of these principles, such as water and the chlorides, have very important functions of a purely physical nature. It is necessary, for example, that the blood should contain a certain proportion of the

chloride of sodium, this substance modifying and regulating the processes of absorption and probably of assimilation. In addition, however, we find the chlorides as constituent parts of every tissue and organ of the body, and so closely united with the nitrogenized principles, that they cannot be completely separated without incineration. Those inorganic matters, the function of which is so marked in their passage through the body, are found largely as constituents of the fluids, and are less abundant in the solids. They are contained in quantity, also, in the liquid excretions; and any excess over the amount actually required by the system is thrown off in this way. Other inorganic matters are especially important as constituent parts of the tissues, and are more abundant in the solids than in the fluids. Examples of principles of this class are the salts of lime, particularly the phosphates. These are also in a condition of intimate union with organic matter, and accompany these principles in all of their so-called vital acts.

If we except certain simple chemical changes, such as the decomposition of the bicarbonates, the inorganic elements of food do not necessarily undergo any modification in the process of digestion. They are generally introduced already in combination with organic matter, and accompany it in the changes which it passes through in digestion, assimilation by the blood, deposition in the tissues, and the final transformations that result in the various excrementitious matters; so that we find the inorganic principles united with the organic matter of the food as it enters the body, and what seem to be the same principles in connection with the organic excrementitious matters; but between these two extremes, are the various operations of assimilation and disassimilation, from which inorganic matter is never absent. We have already referred to these facts so often, under the heads of proximate principles, alimentation, digestion, and excretion, that it is unnecessary, in this connection, to discuss them more fully.

Various combinations of bases with organic acids taken as food, as the acetates, tartrates, etc., found in fruits, undergo decomposition in the body, and are transformed into carbonates. In this form they behave precisely like the other inorganic salts.[1]

Principles consumed by the Organism.

All of the assimilable organic matter taken as food is consumed in the organism; and none is ever discharged from the body, in health, in the form under which it was introduced. The principles thus consumed in nutrition have been divided into nitrogenized and non-nitrogenized; and, although they both disappear in the organism, they possess certain marked differences in their properties, and probably, also, in their relations to nutrition.

Nitrogenized Principles.—The nitrogenized principles, having for their basis, carbon, hydrogen, nitrogen, and oxygen, undergo, in the process of digestion and absorption, remarkable changes; but these are more marked with relation to their properties than their ultimate chemical composition. They are all converted into the nitrogenized elements of the blood, which, in their turn, are transformed into the characteristic nitrogenized principles of the different tissues, and are appropriated by these tissues, to supply the place of worn-out matter. With the intimate nature of this series of transformations, we are entirely unacquainted; but we know that the deposition of new nitrogenized matter in the tissues, constituting one of the most important of the

[1] It is a fact well established that the ingestion of certain salts of vegetable origin produces alkaline carbonates of the same bases, which are discharged in the excretions. The replacement of the vegetable acid in this way by carbonic acid, which is weaker, is supposed by Milne-Edwards to be due to the action of the oxygen in the process of respiration. This explanation is not very satisfactory, but the fact of the production of the alkaline carbonates from the vegetable acid salts cannot be doubted (MILNE-EDWARDS, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 531).

acts of nutrition, is attended with a corresponding loss of matter that has become changed into the nitrogenized elements of excretion. It is the intermediate series of phenomena that is so obscure.

The nutrition of the nitrogenized elements of the tissues may be greatly modified by the supply of new matter. For example, a diet composed of nitrogenized matter in a readily assimilable form will undoubtedly affect favorably the development of the corresponding tissues of the body; and, on the other hand, a deficiency in the supply will produce a corresponding diminution in power and development. The modifications in nutrition due to supply have, however, certain well-defined limits. An excess taken as food is not discharged in the fæces, nor does it pass out in the form in which it entered in the urine; but it apparently undergoes digestion, becomes absorbed by the blood, and increases the quantity of nitrogenized excrementitious matter discharged, particularly the urea. This fact is shown by the great increase in the elimination of urea produced by an excess of nitrogenized food.[1] Whether the nitrogenized matter that is not actually needed in nutrition be changed into urea in the blood, or whether it be appropriated by the tissues, increasing the activity of their disassimilation, is a question difficult to determine experimentally. Certain it is, however, that an excess of nitrogenized food is thrown off in nearly the same way as an excess of inorganic matter; the difference being that the latter passes out in the form in which it has entered, and the former is discharged in the form of nitrogenized excrementitious matter.

Development of Power and Endurance by Exercise and Diet (Training).—The nutrition of the nitrogenized elements of the body is greatly influenced by functional exercise. This is partly local and partly general in its effects. For example, by the persistent exercise of particu-

[1] See page 225.

lar muscles, their development can be carried to a high degree of perfection, the rest of the muscular system undergoing no change; or the entire muscular system may, by appropriate general exercise, be made to increase considerably in volume, and a person may become capable of great endurance, under an ordinary diet. It is surprising, sometimes, to see how small an amount of well-regulated exercise will accomplish this end. But if it be desired to attain the maximum of strength and endurance, it is necessary to carefully regulate the diet as well as the exercise. Those who are in the habit of "training" men, particularly for pugilistic encounters, have long-since demonstrated practically certain facts which physiologists have been rather slow to appreciate. By carefully regulating the diet, confining it chiefly to nitrogenized articles, eliminating fat entirely, and reducing the starchy elements to the minimum; by regulating the exercise so as to increase the nutritive activity of all the muscles to the greatest possible extent; by increasing the respiratory activity by running, etc., and removing from the body all the unnecessary adipose tissue; by all these means, which favor nutritive assimilation by the nitrogenized elements of the organism, a man may be "trained" so as to be capable of immense muscular effort and endurance.

The process of training, skilfully carried out, is in accordance with what are now admitted as physiological laws; though it has been practised for years by ignorant persons, and its rules are entirely empirical. It is stated that the athletes of ancient times, while vigorously exercising the muscles, favored by their diet the development of fat, so as to be better able to resist the blows of their antagonists.[1] However this may be, since the English prize-ring has been regularly organized, or since about the middle of the last century, the system of training has been entirely different, and fat has been, as far as possible, removed from every

[1] HARRISON, *Athletic Training and Health*, Oxford and London, 1869, p. 87.

part of the body. Fat is regarded by trainers as inert matter; and they recognize, practically at least, the fact that the characteristic functions of parts depend for their activity upon their nitrogenized constituents. The contraction of a muscle, for example, is powerful in proportion to the amount and condition of its musculine; and it has been found, practically, that the muscular system can be most thoroughly developed by carefully-graduated exercise and a diet composed largely of nitrogenized matter. In the regular system of training, starch, sugar, fat, and liquids are avoided; and the diet is confined almost entirely to rare meats, eggs, and stale bread or toast, with oatmeal-gruel. The oatmeal has been used from time immemorial, and is supposed to be useful in keeping the bowels in good condition. A very small amount of alcohol and other nervous stimulants, chiefly in the form of home-brewed ale, sherry wine, and tea, are allowed. Sexual intercourse and all unusual nervous excitement are interdicted.

Those who adopt absolutely the classification of food into plastic, or tissue-forming, and calorific, or respiratory, would regard this course of diet as eminently plastic; but during the severe habitual exercise, which is most rigid after the man has been "trained down" so that his fat is reduced to the minimum, the respiratory power and the exhalation of carbonic acid are immensely increased, while the proportion of hydro-carbons in the food is very small.

We do not, of course, propose to discuss from a scientific point of view all of the minutiæ of training. Many of its traditional rules are trivial and unimportant;[1] but it is cer-

[1] A very curious account of training, the more interesting as it contains the essentials of the methods employed at the present day, is to be found in a book on pugilism, called *Boziana*. This work is attributed to the celebrated Captain Barclay (*The Art of Training.—Boxiana; or Sketches of Modern Pugilism, containing all the Transactions of note connected with the Prize-Ring, during the Years* 1821, 1822, 1823, London (no date). The subject of training has attracted considerable attention within the last few years in connection with boating; but the brutal practice of prize-fighting affords, probably, the best examples of strength, endurance, and nervous energy.

tainly a question of great physiological interest to study the processes by which the muscular strength and endurance of a man may be brought to the highest point of development.

One of the most remarkable of the results of thorough training is the development of immense endurance and "wind." This is accomplished by running and prolonged exercise, not so violent as to be exhausting, and always followed by ablutions and frictions, so as to secure a full reaction. The surprising faculty of endurance thus developed must be due in a great measure to nervous power as well as to gradual, careful, and perfectly physiological development of the muscular system. A man may be brought into the ring in what would appear to be perfect condition; but if he be trained down too much or too rapidly, he is liable to give out after comparatively slight exertion. A man who does not possess the required constitutional stamina and nervous power is likely to break down in training, and cannot be brought to proper condition. On the other hand, a man in perfect condition is capable of the maximum of muscular exertion for an hour, or can walk a hundred miles in a day.

It is a question of great importance, in connection with the subject of nutrition, to determine whether the extraordinary muscular power developed by severe training be, in the end, beneficial or deleterious. This can be answered very easily upon practical as well as theoretical grounds. A fully-grown, well-developed man, in perfect health, may be trained so as to be brought to what is technically called fine condition, and he will present at that time all the animal functions in their perfection. He is then a model of a physical man; and the only consequences that can result from such a course are beneficial. The argument that professional pugilists are short-lived is fallacious; for it is well known that almost all of them, after training for and passing through an encounter, immediately relapse into a course of

life, in which all physiological laws are habitually violated. During training, even of the most severe character, not only is great attention paid to diet and exercise, but all of the functions are scrupulously watched. Tranquillity of mind, avoidance of exhaustion, of artificial excitement, stimulants, tobacco, etc., are strictly enjoined; and the process is always very gradual, especially at its commencement, and is continued for several months. The cases in which training has been followed by bad effects are entirely different. Undeveloped boys are frequently trained for boating, in the most reckless manner, until they break down. An attempt is made to accomplish in a few weeks what can only be done physiologically in several months; and the result is, that some of the vital organs, particularly the heart, are liable to become permanently injured. To improve the "wind" and endurance, a person undergoes the most violent exercise, which is followed by great exhaustion, intense respiratory distress, and disturbance of the action of the heart, these vital parts being suddenly forced far beyond their functional capacity. This cannot be done without danger of permanent disturbances of the system, such as have been frequently observed; and it is all the more liable to be followed by bad results, from the fact that amateurs are trained together, five or six under one man, and are more or less independent, while the professional is never out of the sight of his trainer for months, and during that time is under complete control. There is, it seems, every physiological reason to believe that it is beneficial to the general system to bring it to the highest point of functional activity by training; but if this be not done with great caution and judgment, it is liable to be followed by serious results.

Non-Nitrogenized Principles.—The non-nitrogenized principles present a marked contrast to the alimentary substances we have just considered. In the first place, they are not indispensable to the nutrition of all animals. The car-

nivora, for example, may be well nourished upon a diet composed exclusively of nitrogenized matter; and the remarks we have just made upon training show that the human subject may be brought to a high condition of physical development, when starch, sugar, and fat are almost entirely eliminated from the food. This shows conclusively that the division of the food into plastic and calorific elements is not absolute, and that the animal temperature may be maintained without the hydro-carbons. The nitrogenized principles certainly are the only class of alimentary substances capable of forming muscular tissue; but, by certain transformations, with the exact nature of which we are imperfectly acquainted, this class of substances is capable of producing heat and of furnishing the carbonic acid eliminated in respiration. The non-nitrogenized principles are incapable in themselves of meeting the nutritive demands of the system, and they are either consumed without forming part of the tissues, or are deposited in the form of fat. These questions we have already considered fully under the head of alimentation; and it will be remembered that, with a few exceptions, fat always exists in the body uncombined, either in the form of adipose tissue or fatty granulations in the substance of other tissues.

The non-nitrogenized elements taken up by the blood may be divided into two varieties: one, the sugars, composed of carbon with hydrogen and oxygen in the proportions to form water, constituting the true hydro-carbons; and the other, the fats, in which the hydrogen and oxygen do not exist in the proportion to form water. We speak of the sugars only, because starch and all varieties of sugar taken as food are transformed into glucose.

In connection with the study of proximate principles, alimentation, and glycogenesis, we have already referred to the destination of the true hydro-carbons in the organism. They are taken as food to a considerable extent, particularly in the form of starch, and are formed constantly by the liver, in all

classes of animals. Sugar is never discharged from the body in health,[1] nor is it deposited in any part of the organism, even as a temporary condition. It generally disappears in the passage of the blood through the lungs. How is sugar destroyed, and what relation does it bear to nutrition? In studying the changes which it is capable of passing through, it has been found that it may be converted into lactic acid, or be changed into carbonic acid and water; but precisely to what extent the sugars undergo these changes, or how they are acted upon by the inspired oxygen, it has been impossible thus far to determine. We must be content to say that the exact changes which the sugars undergo in nutrition are unknown. They seem very important in development, being abundant in the food and formed largely in the system in early life.[2] They certainly do not enter into the composition of the tissues; and it would seem that they must be important in the two remaining phenomena of nutrition, namely, the formation of fat and the development of animal heat. The relations of sugar to these two processes will be taken up under their appropriate heads.

The fats taken as food are either consumed in the organism, or are deposited in the form of adipose tissue. That the fats are consumed, there can be no doubt; for, in the normal alimentation of man, fat is a constant article, and it is never discharged from the body. We are forced to admit, however, that the changes which fat undergoes in its process of destruction are not thoroughly understood. All that we positively know is, that the fatty principles of the food are formed into a fine emulsion in the small intestine, and are taken up, chiefly by the lacteals, and discharged into the venous system. For a time, during ab-

[1] We have already noted the exceptional discharge of sugar, fat, and nitrogenized matter in the milk.

[2] We have already noted these facts, as well as the production of glycogenic matter and sugar in animals deprived entirely of starch and sugar in their food, when it seems that the formation must take place from the albuminoid principles.

sorption, fat may exist in certain quantity in the blood; but it soon disappears, and is either destroyed directly in the circulatory system, or is deposited in the form of adipose tissue to supply a certain amount of this substance consumed. That it may be destroyed directly is proven by the consumption of fat in instances where the amount of adipose matter is insignificant; and that the adipose tissue of the organism may be consumed is shown by its rapid disappearance in starvation.

The question of the relations of fat to nutrition is important, but somewhat obscure. It does not take part in the nutrition of the parts that are endowed, to an eminent degree, with the so-called vital functions; and when these tissues are brought to their highest point of functional development, the fat is entirely removed from their substance. If fat be not a plastic material, it would seem to have no function remaining but that of keeping up, by its oxidation, the animal temperature. But it is not proven that fat, or fat and sugar, are the sole principles concerned in the production of carbonic acid and the generation of heat; for both of these phenomena occur in the carnivora, and in man, when fat and sugar are eliminated from the food and the fat in the body has been reduced to the minimum. Fat is undoubtedly destroyed in the organism, and probably assists in the formation of the carbonic acid eliminated; it is also taken in much larger proportion in cold than in temperate or warm climates;[1] but we cannot, with our present information, say without reserve, that fats and sugar are oxidized directly, by a process with which we are familiar under the name of combustion, and that their exclusive function is the production of animal heat.

It is a curious fact that fat is generally deposited in tissues during their retrograde processes. The muscular fibres of the uterus, during the involution of this organ after parturition, become the seat of a deposit of fatty granulations.

[1] See vol. ii., Alimentation, p. 128.

Long disuse of any part will produce such changes in its power of appropriating nitrogenized matter for its regeneration, that it soon becomes atrophied and altered. Instead of the normal nitrogenized elements of the tissue, we have, under these circumstances, a deposition of fatty matter. The fat is here inert, and takes the place of the substance that gives to the part its characteristic function. These phenomena are strikingly apparent in muscles that have been long disused or paralyzed, or in nerves that have lost their functional activity. If the change be not too extensive, the fat may be made to disappear, and the part will return to its normal constitution, by appropriate exercise; but frequently the alteration has proceeded so far as to be irremediable and permanent. This condition is known in pathology under the name of fatty degeneration—a term which implies that the nitrogenized elements of the part are changed or degenerated into fat, and which is not strictly correct. During the ordinary process of nutrition, the nitrogenized elements are removed by disassimilation, and new matter, of the same kind, is deposited; but when the so-called fatty degeneration ocures, fat is substituted for the nitrogenized substance. This change, then, should rather be called fatty substitution.[1]

Accurate observations have shown that, in young animals, rapidly fattened, all the adipose matter in the body cannot be accounted for by what is taken in as food; and it is certain that fat may be produced *de novo* in the organism.

Formation and Deposition of Fat.—The question of the generation of fat in the economy is one of great importance. Whatever the exact nature of the changes accompanying the destruction of non-nitrogenized matter may be, it is certain that the fat stored up in the body is consumed, when there is a deficiency in any of the elements of food, as well as that which is taken into the alimentary canal. It is

[1] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, p. 1444, Article, *Substitution graisseuse.*

rendered probable, indeed, by the few experiments that have been made on the subject, that obesity increases the power of resistance to inanition.[1] At all events, in starvation, the fatty constituents of the body are the first to be consumed, and they almost entirely disappear before death. As we have already seen, sugar is never deposited in any part of the organism, and is only a temporary constituent of the blood. If the sugars and fats have, in certain regards, similar functions in nutrition, and if, in addition to the mechanical functions of fat, it may be retained in the organism for use under extraordinary conditions, it becomes very important to ascertain the mechanism of its production and deposition.

The production of fatty matter by certain insects, in excess of the fat supplied with the food, was established long ago by the researches of Huber, whose experiments were fully confirmed by Dumas and Milne-Edwards.[2] A little later, similar observations were made upon birds, by Persoz,[3] and upon birds and mammals, by Boussingault.[4] Some of the experiments of Boussingault are peculiarly interesting, as they were made upon pigs, in which the digestive apparatus closely resembles that of the human subject. They showed conclusively that, under certain circumstances, more fat exists in the bodies of animals than can be accounted for by the total amount of fat taken as food added to the fat existing at birth. In some very interesting experiments with relation to the influence of different kinds of food upon the development of fat, it was ascertained that fat could be produced in animals upon a regimen, sufficiently nitrogenized, but deprived of fatty matters; but the fact should be recog-

[1] See vol. ii., Alimentation, p. 26.

[2] Milne-Edwards, *Leçons sur la physiologie*, Paris, 1862, tome vii., p. 553.

[3] Persoz, *Expériences sur l'engrais des oies.—Comptes rendus*, Paris, 1844, tome xviii., p. 245.

[4] Boussingault, *Recherches expérimentales sur le developpement de la graisse pendent l'alimentation des animaux.—Mémoires de chimie agricole et de physiologie*, Paris, 1854, p. 105, *et seq.*

nized "that the nutriment which produces the most rapid and pronounced fattening is precisely that which joins to the proper proportion of albuminoid substances the greatest proportion of fatty principles."[1]

Animals cannot be fattened without a certain variety in the regimen. We have already discussed the necessity of a varied diet, and have shown that an animal will die of starvation when confined exclusively to one class of principles, even if this be of the most nutritious character;[2] and it is not necessary to refer again to the experiments which have demonstrated that a diet confined exclusively to starch, sugar, or fat, or even pure albumen or fibrin, cannot sustain life, much less fatten an animal. We are prepared, then, to understand why, in the pigs experimented upon by Boussingault, a regimen confined to potatoes did not prove to be fattening, notwithstanding the large proportion of starch,[3] and that fat was produced in abundance only when the food presented the proper variety of principles.

Very little is known concerning the precise mechanism of the production of fat. The experiments of Boussingault seem to leave no doubt that it may be formed from any kind of food, even when it is exclusively nitrogenized;[4] but it is, nevertheless, a matter of common observation that certain articles of diet are more favorable to its deposition than others; and it is also true that the herbivora are fattened much more readily, as a rule, than the carnivora.

Theoretical considerations would immediately point to starch and sugar as the elements of food most easily convertible into fat, as they contain the same elements, though in different proportions; and it is more than probable that

[1] BOUSSINGAULT, *op. cit.*, p. 167.

[2] See vol. ii., Alimentation, p. 128.

[3] *Op. cit.*, p. 122.

[4] The researches of Wurtz have shown that certain of the albuminoid principles can be converted into fatty acids by the action of an alkali and heat, and that this may also occur spontaneously (WURTZ, *Sur la transformation de la fibrine en acide butyrique.—Comptes rendus*, Paris, 1844, tome xviii., p. 704).

this view is correct. It is said that in sugar-growing sections, during the period of grinding the cane, the laborers become excessively fat, from eating large quantities of the saccharine matter. We cannot refer to any exact scientific observations on this point, but the fact is pretty generally admitted by physiologists. Again, it has been frequently a matter of individual experience that sugar and starch are favorable to the deposition of fat, especially when there is a constitutional tendency to obesity. A most remarkable example of this, and one which has met with considerable notoriety, is worthy of mention, though not reported by a scientific observer. We refer to the letter on corpulence, by Mr. Banting.[1] The writer of this curious pamphlet, in 1862, was sixty-six years old, five feet and five inches in height, and weighed two hundred and two pounds. Under the advice of Mr. William Harvey, F. R. C. S., of London, he confined himself to a diet containing no sugar, and as little starch and fat as possible. Continuing this regimen for one year, he gradually lost weight, at the rate of about one pound each week, until he was reduced to one hundred and fifty-six pounds. At the time the last edition of the pamphlet was published, in 1864, he enjoyed perfect health and weighed one hundred and fifty pounds, his weight varying only to the extent of one pound, more or less, in the course of a month. This little tract is very interesting, both from the importance of its physiological relations and its quaint literary style. It has had an immense circulation, and many persons suffering from excessive adipose development have adopted the system here advised, with results more or less favorable. A study of the course of diet here prescribed shows it be a pretty rigid training system, with the exception of succulent vegetables and liquids, which are allowed without restriction. It is proper to remark, however, that some enthusiastic advocates of the plan have exceeded the limits prescribed, and neglected the caution of the author

[1] BANTING, *Letter on Corpulence*, London, 1864.

always to employ it under the advice of a physician; and its too rigid enforcement has been followed by serious disturbances in general nutrition. Others, however, have verified the favorable results obtained by Mr. Banting.

It is difficult to explain the remarkable constitutional tendency to obesity observed in some individuals, which is very often hereditary. Such persons will become very fat upon a comparatively low diet, while others deposit but little adipose matter, even when the regimen is abundant. It is to be noted, however, that the former are generally addicted to the use of starchy, saccharine, and fatty elements of food, while the latter consume a greater proportion of nitrogenized matter.

It is not an uncommon remark that the habit of taking large quantities of liquids favors the formation of fat; but it is not easy to find any scientific basis for such an opinion. As to the formation of fat by any particular organ or organs in the body, no positive scientific view has been advanced, except the proposition by Bernard, that the liver had this function, in addition to its glycogenic office. This we have already discussed, and have shown that such a function is far from being positively established.[1]

Condition under which Fat exists in the Organism.—It is said that fat combined with phosphorus is united with nitrogenized matter in the substance of the nervous tissue; but its condition here is not well understood, as we shall see when we come to treat of the nervous system. A small quantity of fat is contained in the blood-corpuscles, and a little is held in solution in the bile; but with these exceptions, fat always exists in the body isolated and uncombined with nitrogenized matter, in the form of granules or globules and of adipose tissue. The three varieties of fat are here combined in variable proportions, which is the cause of the differences in its consistence in different situations. The ultimate ele-

[1] See page 328.

ments of fat are, carbon, hydrogen, and oxygen, the two latter in unequal proportions. It has been found very difficult, however, to obtain either stearine, margarine, or oleine in a condition of sufficient purity to ascertain their exact ultimate composition.[1]

Physiological Anatomy of Adipose Tissue.—Adipose tissue is found in abundance in the interstices of the subcutaneous areolar tissue, where it is sometimes known as the panniculus adiposus. It is not, however, to be confounded with the so-called cellular or areolar tissue, and is simply associated with it without being one of its essential parts; for the areolar tissue is abundant in certain situations, as the eyelids and scrotum, where there is no adipose matter, and adipose tissue exists sometimes, as in the marrow of the bones, without any areolar tissue.

Adipose tissue is widely distributed in the body, and has important mechanical functions.[2] Its anatomical element is a vesicle, from $\frac{1}{800}$ to $\frac{1}{300}$ of an inch in diameter, composed of a delicate, structureless membrane, $\frac{1}{25000}$ of an inch thick, enclosing fluid contents.[3] The form of the vesicles is naturally rounded or ovoid; but in microscopical preparations they are generally compressed so as to become irregularly polyhedrical. The membrane sometimes presents a small nucleus attached to its inner surface. The contents are a minute quantity of an albuminoid fluid moistening the internal surface of the membrane, and a mixture of oleine, margarine, and stearine, liquid at the temperature of the body, but becoming harder on cooling.[4] Little rosettes formed of acicular crystals of margarine are frequently observed in the fat-vesicles, when the temperature is rather low.

[1] ROBIN ET VERDEIL, *Traité de chimie anatomique et physiologique*, Paris, 1853, tome iii., p. 105.

[2] See vol. i., Introduction, p. 65.

[3] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Adipeux*.

[4] TODD AND BOWMAN, *Physiological Anatomy and Physiology of Man*, Philadelphia, 1857, p. 89.

The adipose vesicles are collected into little lobules, from $\frac{1}{50}$ to $\frac{1}{4}$ of an inch in diameter,[1] which are surrounded by a rather wide net-work of capillary blood-vessels. Close examination of these vessels shows that they frequently surround individual fat-cells, in the form of single loops. There is no distribution of nerves or lymphatics to the elements of adipose tissue.

It is seen by this sketch of the structure of adipose tissue, that there is no anatomical reason for classing these vesicles with the ductless glands, as is done by some physiologists. They undoubtedly, under certain conditions, have the power of filling themselves with fat; but it would be no more appropriate to call this a secretion than to apply this term to the development and nutrition of the muscular substance within the sarcolemma.

Conditions which influence Nutrition.—We know more concerning the conditions that influence the general process of nutrition than about the nature of the process itself. It will be seen, for example, when we come to study the nervous system, that there are nerves which regulate, to a certain extent, the nutritive forces. We do not mean to imply that nutrition is effected through the influence of the nerves, but it is the fact that certain nerves, by regulating the supply of blood, and perhaps by other influences, are capable of modifying the nutrition of parts to a very considerable extent.

In discussing the influence of exercise upon the development of parts, we have shown that this is not only desirable but indispensable; and the proper performance of the functions of all parts involves the action of the nervous system. It is true that the separate parts of the organism and the organism as a whole have a limited existence; but it is not true that the change of nitrogenized, living substance into effete matter, a process that is increased in activity by phys-

[1] Littré et Robin, *loc. cit.*

iological exercise, consumes, so to speak, a definite amount of the limited life of the part. Physiological exercise increases disassimilation, but it also increases the activity of nutrition and favors development. It is a favorite sophism to assert that bodily or mental effort is made always at the expense of a definite amount of vitality and matter consumed. This is partly true, but mainly false. Work involves change into effete matter; but when restricted within physiological limits, it engenders a corresponding activity of nutrition, assuming, of course, that the supply from without be sufficient. Other things being equal, a man will live longer under a system of physiological exercise of every part, than if he made the least effort possible. It is, indeed, only by such use of parts that they can undergo proper development and become the seat of normal nutrition. But notwithstanding all these facts, life is self-limited. Unless subjected to some process which arrests all changes, such as cold, the action of preservative fluids, etc., organic substances are constantly undergoing transformation. In the living body, their disassimilation and nutrition are unceasing; and after they are removed from the influence of what is called life, they change, first losing irritability, or becoming incapable of performing their functions, and afterward decomposing into matters which, like the results of their disassimilation, are destined to be appropriated by the vegetable kingdom. Nutrition sufficient to supply the physiological decay of parts cannot continue indefinitely. The wonderful forces in the fecundated ovum lead it through a process of development that requires, in the human subject, more than twenty years for its completion; and when development ceases, no one can say why it becomes arrested, nor can we give any sufficient reason why, with a sufficient and appropriate supply of material, a man should not grow indefinitely. After the being is fully developed, and during what is known as the adult period, the supply seems to be about equal to the waste. But after this, nutrition gradually becomes deficient,

and the deposition of new matter in progressive old age is more and more inadequate to supply the place of the living nitrogenized substance. We may at this time, as an exception, have a considerable deposition of fat, but the nitrogenized matter is always deficient, and the proportion of inert inorganic matter combined with it is increased.

There can be little if any doubt that the forces which induce the regeneration or nutrition of parts reside in the organic nitrogenized substance, and that they give to the parts their characteristic functions, which we call vital; the inorganic matter being passive, or having, at the most, purely physical functions. If, therefore, as age advances, the organic matter be gradually losing the power of completely regenerating its substance, and if its proportion be progressively diminishing, while the inorganic matter is increasing in quantity, a time will come when some of the organs necessary to life will be unable to perform their office. When this occurs we have death from old age, or physiological dissolution. This may be a gradual failure of the general process of nutrition, or it may attack some one organ or system. Why death is thus certain tc occur, we do not know, any more than we can explain why and how animals live.

The modifications in nutrition due to the very varied influences that may be brought to bear upon it present a most extended subject for discussion; but we shall not touch upon any of these influences that are not purely physiological. Among the most interesting of these modifications, are those due to age, constituting, as they do, in early life, the process of development. They will be treated of fully in connection with the subject of generation. It is evident, also, from what we have already said, that each tissue and organ has its own conditions of nutrition and development; and this constitutes another interesting division of the subject, the more so, because the nutrition and development of the individual tissues are closely connected with the processes of

regeneration and repair after injury. We have stated, as far as possible, all that is positively known of the nutrition of the fully-formed tissues of the body; but their development belongs to embryology. If we were to attempt to follow the processes of regeneration after injury in nerves, muscles, bone, etc., we would be compelled to pass almost immediately into the domain of pathology. The influences of climate, respiratory activity, food, etc., have already been considered under the heads of respiration, alimentation, and excretion, and will be touched upon again in connection with animal heat.

Products of Disassimilation.—It only remains now to recapitulate briefly the mode of production of the excretions. The process of disassimilation, we are aware, always accompanies nutrition, and the substances thus formed are the result of the final changes of the organic constituents of the tissues. As we have seen in studying the urine, the excrementitious principles proper are always associated with inorganic matter, which has passed through the organism; and while there are many effete substances that we have been able to recognize, there are probably others which have thus far escaped observation. It is almost futile to speculate upon the probable bearing which the discovery of new excrementitious principles will have upon pathological conditions, while there are so many, which we now know only by name, their relations to the different tissues being still obscure; but if we reason from the light thrown upon certain diseased conditions by the fact that urea, the urates, and cholesterine are liable to be retained in the blood and produce certain symptoms, we may safely infer that the description of new effete principles will have an important influence upon our pathological knowledge as well as our comprehension of physiological processes. The following are the most important excrementitious matters, the relations of which to nutrition and disassimilation are more or less fully understood:

Products of Disassimilation.

Name of principle.	*How excreted.*
Carbonic acid (CO_2)	Principally by the lungs; but also by the skin, and in solution in the excreted fluids.
Alkaline sudorates (Sudoric acid, $C_{10}H_8O_{13}N$)	Perspiration.
Urea ($C_2H_4N_2O_2$)	Principally in the urine; but a certain quantity in the perspiration.
Urate of soda (Uric acid, $C_5HN_2O_3+HO$)	Urine.
Urate of ammonia	"
Urate of potassa	"
Urate of lime	"
Urate of magnesia	"
Hippurate of soda (Hippuric acid, $C_{18}H_9NO_6$)	"
Hippurate of potassa	"
Hippurate of lime	"
Creatine ($C_8H_9O_4N_3+2HO$)	"
Creatinine ($C_8H_7O_2N_3$)	"
Oxalate of lime (CaO,C_2O_3+2HO)	"
Xanthine ($C_{10}H_4N_4O_4$)	"
Stercorine (changed from Cholesterine, $C_{25}H_{22}O$, of bile)	Fæces.
Excretine ($C_{78}H_{78}O_2S$)	"

In the above list we have omitted all doubtful excrementitious principles, as well as the inorganic compounds found in the excreted fluids; and we can safely assume that the substances therein enumerated represent, as far as we are now able to determine, the physiological wear of the organism. We shall not again discuss the fact that the life of tissues involves physiological waste or decay, and that the excrementitious principles proper represent the final changes of the organic substance. We know that this process goes on without necessarily involving exercise of the peculiar functions of the parts; but it is no less true that exercise, or work, increases the activity both of nutrition and wear. This is one of the great principles underlying all our ideas

of the process of nutrition. We shall not discuss here the influence of work upon the elimination of some of the nitrogenized compounds, particularly urea, for we have already examined that subject most carefully in another place;[1] but we have no hesitation in stating, as a general law, that has yet to find its exceptions, that physiological work increases excretion.

[1] See page 226.

CHAPTER XIII.

ANIMAL HEAT.

General considerations—Limits of variation in the normal temperature in man—Variations with external temperature—Variations in different parts of the body—Variations at different periods of life—Diurnal variations—Relations of animal heat to digestion—Influence of defective nutrition and inanition—Influence of exercise, mental exertion, and the nervous system, upon the heat of the body.

THE process of nutrition in animals is always attended with the development of heat, and produces a temperature more or less independent of external conditions. This is true in the lowest as well as the highest animal organizations; and analogous phenomena have even been observed in plants. In cold-blooded animals, nutrition may be suspended by a diminished external temperature, and certain of the functions become temporarily arrested, to be resumed when the animal is exposed to a greater heat. This is true, to some extent, in certain warm-blooded animals that periodically pass into a condition of stupor, called hibernation; but in man, and nearly all the warm-blooded animals, the general temperature of the body can undergo but slight variations. The animal heat is essentially the same in the intense cold of the frigid zones and under the burning sun of the tropics; and if, from any cause, the body become incapable of keeping up its temperature when exposed to cold, or moderating it when exposed to heat, death is the invariable result.

The production of animal heat is so closely connected with nutrition, that in serious pathological modifications of

this process, as in the essential fevers or extensive inflammations, the temperature of the body becomes an important guide, particularly in prognosis. The clinical value of a recognition of the temperature in disease has only been fully appreciated within a few years, especially since the very elaborate observations of Wunderlich, and other German observers.[1]

The study of the temperature in different classes of animals presents very great interest, but the limits of a work on pure human physiology restrict us to the phenomena as observed in man, and in animals in which the processes of nutrition are similar, if not identical. We shall therefore treat of the subject from one point of view, and consider it as follows:

1. The normal temperature in the human subject, with its variations in different parts of the body and at different periods of life.

2. The diurnal variations in the animal temperature, and the relations of alimentation, digestion, respiration, nutrition, exercise, and the nervous system.

3. The means by which the temperature of the body is kept within the limits necessary to the preservation of life and health.

Limits of Variation in the Normal Temperature in Man.—A great number of observations have been made upon the normal temperature in the human subject under different conditions; but we shall cite those only in which all sources of error in thermometry seem to have been avoided, and in which the results present noticeable peculiarities. One of the most common methods of taking the general temperature has been to introduce a delicate thermometer, carefully protected from all disturbing conditions, into the axilla, reading off the degrees after the mercury has become abso-

[1] HIRTZ, *Chaleur dans l'état de maladie.—Nouveau dictionnaire de médecine*, Paris, 1867, tome vi., p. 772, *et seq.*

lutely stationary. Nearly all observations made in this way agree with the results obtained by Gavarret,[1] who estimates that the temperature in the axilla, in a perfectly healthy adult man, in a temperate climate, ranges between 97·7° and 99·5°.[2] Dr. Davy, from a large number of observations on the temperature under the tongue, estimates the standard, in a temperate climate, at 98°.[3] When we examine the temperature of the blood in the deeper vessels and the variations in different parts, we shall see that the axilla and the tongue, being more or less exposed to external influences, do not exactly represent the general heat of the organism; but these are the situations, particularly the axilla, in which the temperature is most frequently taken, both in physiological and pathological examinations. As a standard for comparison, we may assume that the most common temperature in these situations is 98°, subject to variation within the limits of health of about 0·5° below and 1·5° above.

Variations with External Temperature.—There can be no doubt that the general temperature of the body varies, though within very restricted limits, with extreme changes in climate. The results obtained by Davy, in a large number of observations in temperate and hot climates, show an elevation in the tropics of from 0·5° to 3°.[4] It is well known, also, that the human body, the surface being properly protected, is capable of enduring for some minutes a heat much greater than that of boiling water. Under these conditions, the general temperature is raised but very slightly, as compared with the intense heat of the surrounding atmosphere According to the observations of Dr. Dobson, the temperature was only raised to 99·5° in one instance, 101·5° in an-

[1] GAVARRET, *De la chaleur produite par les êtres vivants*, Paris, 1855, p. 100.

[2] All the temperatures, unless it be otherwise stated, are given according to the Fahrenheit scale.

[3] DAVY, *Researches, Physiological and Anatomical*, London, 1839, vol. i., p. 196.

[4] DAVY, *loc. cit.*

other, and 102° in a third, when the body was exposed to a heat of more than 212°.[1] MM. Delaroche and Berger, however, found that the temperature in the mouth could be increased by from 3° to 9°, after sixteen minutes' exposure to intense heat.[2] This was for the external parts only; but it is not at all probable that the temperature of the internal organs ever undergoes such extensive variations.

It is very difficult to estimate the temperature in persons exposed to intense cold, as in Arctic explorations, because the greatest care is always taken to protect the surface of the body as fully as possible; but experiments have shown that the animal heat may be considerably reduced, as a temporary condition, without producing death. In the latter part of the last century, Dr. Currie caused the temperature in a man to fall 15° by immersion in a cold bath; but he could not bring it below 83°. This extreme depression, however, lasted only two or three minutes, and the temperature afterward returned to within a few degrees of the normal standard.[3] Nearly the same results were obtained by Hunter, in a series of experiments on a mouse. With an external temperature of 60°, he found the temperature in the upper part of the abdomen 99°, and in the pelvis 96°. The animal was then exposed for an hour to a cold

[1] DOBSON, *Experiments in an Heated Room.—Philosophical Transactions*, London, 1775, p. 463, *et seq.*

[2] DELAROCHE, *Expériences sur les effets qu'une forte chaleur produit dans l'économie animale.—Thèses de Paris*, 1806, tome i., No. xi. M. Delaroche, in connection with M. Berger, made a number of very interesting experiments upon the influence of high temperatures upon the general heat of the body. Delaroche remained for eight minutes exposed to a temperature of 176°, and the temperature under the tongue was raised from a little over 98° to nearly 107°. In an experiment of the same kind by Berger, the temperature was raised, in sixteen minutes, from 98° to nearly 105°. Enclosed in a hot steam-bath of from 100° to 120°, the temperature, in one instance, was raised, in thirteen minutes, to over 103°, and in another, in fifteen minutes, to 101° (*Loc. cit.*, pp. 43, 44).

[3] CURRIE, *An Account of the remarkable Effects of a Shipwreck on the Mariners; with Experiments and Observations on the Influence of Immersion in fresh and salt Water, hot and cold, on the Powers of the living Body.—Philosophical Transactions*, London, 1792, p. 204, *et seq.*

atmosphere of 13°, and there was a diminution of the temperature at the diaphragm of 16°, and at the pelvis of 18°.[1]

These results show that while the normal variations in temperature in the human subject, even when exposed to great climatic changes, are very slight, generally not ranging beyond two degrees, the body may be exposed for a time to excessive heat or cold, and the extreme limits, consistent with the preservation of life, may be reached. As far as has been ascertained by direct experiment, these limits are 83° and 107°; giving a range of about 15° below and 9° above the average standard under normal conditions.[2]

Variations in different Parts of the Body.—It is to be expected that the temperature of the internal organs should be higher and more constant than that of parts, like the axilla or mouth, more or less exposed to loss of heat by evaporation and contact with the cool air; and the differences observed in the blood in certain parts, as in the two sides of the heart, have important bearings, as we shall hereafter show, upon the various theories of animal heat. We shall here simply note the variations observed in the blood in different situations, and confine ourselves chiefly to late observations, which have generally been made with apparatus much more reliable and delicate than was formerly employed.

A great number of experiments have been made upon modifications in temperature accompanying the general change of the blood from arterial to venous; but perhaps the most exact and elaborate are those by M. Claude Bernard. For measuring the temperature in different parts of the vascular system, he used the exceedingly delicate "me-

[1] HUNTER, *Observations on certain Parts of the Animal Œconomy*, London, 1792, p. 114.

[2] We have referred only to observations upon the influence of the surrounding temperature in man and mammals generally. Certain important peculiarities in this regard have been observed in hibernating animals, and in reptiles, fishes, and insects, the consideration of which belongs to comparative physiology.

tastatic" thermometers of M. Walferdin;[1] and in all comparative observations he employed the same instrument, introduced successively into different parts, frequently reversing the order, and employing every precaution so as to insure perfectly physiological conditions. The preëminent skill of this distinguished observer in experimenting upon living animals is almost in itself a sufficient guarantee of the accuracy of his results.

It is universally admitted that the blood becomes slightly lowered in its temperature in passing through the general capillary circulation;[2] but the amount of difference is ordinarily not more than a fraction of a degree, and is dependent, in all probability, upon external conditions and the evaporation constantly going on from the surface of the body. This fact is not at all opposed to the proposition that the animal heat is generated in greatest part in the general capillary system, as one of the results of nutritive action; for the blood circulates with such rapidity that the heat acquired in the capillaries of the internal organs, where little or none is lost, is but slightly diminished before the fluid passes into the arteries, even in circulating through the lungs; and the evaporation from the surface simply moderates the heat acquired in the tissues, and keeps it at the proper standard. We know that the heat of the body is equalized by means of the circulation and cutaneous transpiration; and all comparative observations on the temperature in different parts show that, where it is not subjected to refrigerating influences, the blood is warmer in the veins than in the arteries.

The elaborate investigations of Bernard have demonstrated that the blood is, as the rule, from 0·36° to 1·8° warmer in the hepatic veins than in the aorta. The temperature in the hepatic veins is from 0·18° to 1·44° higher

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome i., p. 67, *et seq.* Bernard here gives a full description of this instrument. With it he has been able to note accurately variations of $\frac{1}{100}$ of a degree cent.

[2] BERNARD, *op. cit.*, p. 58, and LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 517.

than in the portal veins. These figures are the result of numerous experiments made on dogs. The maximum of thirty-three observations upon the temperature in the aorta was 105·8°, and the minimum, 98·78°; the maximum of thirty-two observations upon the portal vein was 106·34°, and the minimum, 100·04°; the maximum of thirty-five observations upon the hepatic veins was 107°, and the minimum, 99·86°.[1] Compared with the aorta, the temperature of the portal vein was generally found to be higher (maximum of difference, 0·9°); but in a few instances, five out of fifteen, it was a very little lower, which is explained by Bernard by the supposition that the intestinal canal is not entirely removed from external modifying influences. These results show that the blood coming from the liver is warmer than in any other part of the body.

The general fact that the superficial parts are cooler than those less exposed to loss of heat by evaporation, observed by Hunter,[2] Davy,[3] and others, does not demand extended discussion; but in a series of experiments by Breschet and Becquerel,[4] who were among the first to employ thermo-electric apparatus in the study of animal heat, it was found that the cellular tissue was from 2·5° to 3·3° cooler than the muscles. This difference will be readily understood when we consider the production of heat in the general system, and more especially in the highly-organized parts.

A most interesting question, in this connection, relates

[1] BERNARD, *op. cit.*, p. 84. We have calculated these results from an elaborate table given by Bernard, but have disregarded two observations (Nos. 17 and 18, table iii.), made on animals after death, the circulation being kept up by artificial respiration.

[2] HUNTER, *Experiments and Observations on Animals, with respect to the Power of producing Heat.—Observations on certain Parts of the Animal Œconomy*, London, 1792, pp. 108, 115.

[3] DAVY, *Researches, Physiological and Anatomical*, London, 1839, vol. i., p. 150, *et seq.* The paper here referred to first appeared in the *Philosophical Transactions*, in 1814.

[4] BRESCHET ET BECQUEREL, *Premier mémoire sur la chaleur animale.—Annales de chimie et de physique*, Paris, 1835, tome lix., p. 129.

to the comparative temperature of the blood in the two sides of the heart. Upon this point there have been several conflicting observations, the results favoring two opposite theories of calorification. By some it has been thought that the blood gains heat in passing through the lungs, and this is explained by the theory of the direct union, in these organs, of oxygen with the hydro-carbons; while others suppose that the blood is slightly refrigerated in the air-cells. The questions here involved will be fully discussed in connection with the theories of animal heat; and we shall confine ourselves at present to a study of the experimental facts.

An excellent review of all the important direct observations upon the temperature of the two sides of the heart in living animals is given by Bernard, as an introduction to his original experiments. It appears from this that Coleman, Astley Cooper, Saissy, Davy, Thackrah, and Nasse, found the blood warmer in the left side of the heart than in the right. Mayer did not find any difference in animals recently killed. Autenreith found the blood warmer in the right side in an animal recently killed, the circulation being kept up by artificial respiration. Berger, Collard de Martigny, Magendie and Bernard, Hering, Georg von Liebig, and Fick found a marked difference in favor of the right side.[1] This being the state of the question in 1859, it remains to see how far the conditions under which these results were obtained are capable of explaining their contradictory character.

It is evident that, when the chest is opened, the external refrigerating influences might act differently upon the two sides of the heart, particularly as the right ventricle is much thinner than the left. It would not be improper, indeed, to exclude all observations made in this way, and depend entirely upon experiments in which the physiological conditions are not so palpably violated. Magendie and Bernard introduced delicate thermometers into the two sides of the

[1] BERNARD, *Liquides de l'organisme*, Paris, 1859, tome i., p. 55, *et seq.*

heart, through the vessels in the neck, without opening the chest. These experiments were made upon a horse, and the right heart was always found considerably warmer than the left. Hering introduced a thermometer into the cavities of the heart in a living calf affected with cardiac ectopia. The temperature of the right side was 102·74°, and the left side, 101·79°.[1] Georg von Liebig illustrated one of the sources of error in all examinations made after opening the chest, by filling the cavities of the heart of a dog with warm water, placing the organ in a water-bath, and bringing the two sides to precisely the same temperature. After five minutes' exposure to the air, the temperature in the right ventricle was sensibly lower than in the left, which was undoubtedly due to the difference in the thickness of the walls.[2] The observations by Bernard himself upon dogs and sheep are very conclusive, as far as these animals are concerned. In dogs he found a difference of from 0·1° to 0·2°, always in favor of the right side; and the results in sheep were nearly the same.[3]

A series of experiments recently instituted by Colin shows pretty conclusively that there are other conditions that may account, in a measure, for the opposite results of observations on the temperature of the two sides of the heart, besides exposure of the parts to the air. In one hundred and two experiments, he found the blood warmer in the right side in thirty-one; in fifty-one, it was warmer on the left side; and in twenty-one, there was no difference.[4] He finds that in animals covered with a thick fleece, like sheep, where there is but little loss of temperature by the general surface, the blood in the right heart is generally

[1] BERNARD (*op. cit.*, p. 106, *et seq.*) gives a full account of this very interesting observation.

[2] BERNARD, *op. cit.*, p. 65.

[3] *Op. cit.*, pp. 110, 116.

[4] COLIN, *Expériences sur la chaleur animale*, in the report by LONGET.—*Comptes rendus*, Paris, 1867, tome lxiv., p. 464. The error in the figures quoted is in the original report.

warmer than in the left; while in horses, dogs, and probably in man, where there is considerable loss of heat by the skin, the blood is warmer on the left side. It is difficult to explain how the blood can pass through the lungs without losing a certain amount of heat, but the experiments just detailed, taken in connection with some of the earlier observations, leave little doubt as to the fact.

These experiments are only indirectly applicable to the human subject; and if it be proven that in animals, the conditions vary with "the state of the skin, the digestive apparatus, and the muscular system,"[1] it is impossible, in the absence of positive demonstration, to say what change in temperature, if any, takes place in the blood in its passage through the lungs. The only reliable observations upon this point in man are those lately made by Prof. Lombard, of Boston. Prof. Lombard used in his experiments a very ingenious and delicate thermo-electric apparatus, capable of indicating a difference of $\frac{1}{2000}$ of a degree cent.[2] With this instrument, he was able to determine very slight variations in the temperature of the blood in the arterial system, by simply placing the conductors over any of the superficial vessels, like the radial. Of course it is impossible to note the actual temperature in the two sides of the heart in the human subject during life; but Prof. Lombard endeavored to arrive at the same end, by calculating that if all the sources of refrigeration in the lungs were artificially removed, the blood in the arteries should gain about the same amount of heat that would be lost under ordinary conditions. To effect this object, he breathed air saturated with moisture and of the same temperature as the circulating blood. "If, then, when respiration takes place under ordinary circumstances, the blood is cooled one-third of a degree (cent.) in passing through the lungs, the temperature should

[1] COLIN, *loc. cit.*

[2] LOMBARD, *Description d'un nouvel appareil thermo-électrique pour l'étude de la chaleur animale.—Archives de physiologie*, Paris, 1868, tome i., p. 498.

be raised so much; that is to say, one-third of a degree, when we respire air at the temperature of the blood and saturated with the vapor of water, all loss of heat then being impossible."[1] In numerous experiments performed on this principle, Prof. Lombard failed to observe a sufficiently marked elevation of temperature to justify the conclusion that the blood is ordinarily cooled in passing through the lungs. These experiments cannot be so positive as those made by introducing thermometers into the heart in living animals without opening the chest or disturbing the circulation; but they are important, in connection with such observations, as failing to prove that the blood is either cooled or heated in the lungs.

From these facts it appears that there is no positive evidence of any change in the temperature in the blood in passing through the lungs in the human subject. In animals there probably exist no constant differences in temperature in the two sides of the heart. When the loss of heat by the general surface is active, as in animals with a slight covering of hair, the blood is generally cooler in the right cavities; but in animals with a thick covering, that probably lose a great deal of heat by the pulmonary surface, the blood is cooler on the left side. There can be no doubt that there are refrigerating influences in the lungs, both from the low temperature of the inspired air and evaporation; but these are equalized and sometimes overcome by processes in the blood itself; although, as we shall see hereafter, the lungs are by no means the most important organs of calorification.

Variations at different Periods of Life.—The most important variations in the temperature of the body at different periods of life are observed in infants just after birth. Aside from one or two observations, which are admitted to be ex-

[1] LOMBARD, *Recherches expérimentales sur l'influence de la respiration sur la température du sang dans son passage à travers le poumon.—Archives de physiologie*, Paris, 1869, tome ii., p. 7.

ceptional, the body of the infant and of young mammalia and birds, removed from the mother, presents a diminution in temperature of from one to nearly four degrees. This important fact was established by W. F. Edwards,[1] who made, also, a number of curious and instructive experiments upon the power of young warm-blooded animals to resist cold. In infancy the ability to resist cold is less than in later years; but after a few days the temperature of the child nearly reaches the standard in the adult, and the variations produced by external conditions are less considerable. These facts have been fully confirmed by the researches of Despretz,[2] Roger,[3] and others.

The experiments of W. F. Edwards have an important bearing upon our ideas of nutrition during the first periods of extra-uterine life. He found that in certain animals, particularly dogs and cats, that are born with the eyes closed and in which the foramen ovale remains open for a few days, the temperature rapidly diminished when they were removed from the body of the mother, and that they then become reduced to a condition approximating that of cold-blooded animals; but after about fifteen days, this change in temperature could not be effected. In dogs just born, the temperature fell after three or four hours' separation from the mother to a point but a few degrees above that of the surrounding atmosphere.[4] The views advanced by Edwards are fully illustrated in instances of premature birth, when the animal heat is much more variable than in infants at

[1] W. F. Edwards, *De l'influence des agens physiques sur la vie*, Paris, 1824, p. 234.

[2] Despretz, *Recherches expérimentales sur les causes de la chaleur animale.—Annales de chimie et de physique*, Paris, 1824, tome xxvi., p. 338. Despretz found the temperature in three infants, between one and two days old, only 95·1°.

[3] Roger, *De la température chez les enfants à l'état physiologique et pathologique.—Archives générales de médecine*, Paris, 1845, 4me série, tome ix., p. 264.

[4] *Op. cit.*, p. 132, *et seq.*

term,[1] and in cases of persistence of the foramen ovale. In certain instances in which life has been prolonged under this abnormal condition, the individual is nearly in the condition of a cold-blooded animal. We can also understand the remarkable power of resistance to asphyxia in newly-born animals observed by Buffon, Legallois, and Edwards;[2] for it is well known that cold-blooded animals will bear deprivation of oxygen much better than the higher classes.

In adult life there does not appear to be any marked and constant variation in the normal temperature; but in old age, according to the observations of Davy, while the actual temperature of the body is not notably reduced, the power of resisting refrigerating influences is diminished very considerably.[3]

There are no positive observations showing any constant differences in the temperature of the body in the sexes; and it may be assumed that in the female, the animal heat is modified by the same influences and in the same way as in the male.

Diurnal Variations in the Temperature of the Body.—Although the limits of variation in the animal temperature are not very extended, certain fluctuations are observed, depending upon repose or activity, digestion, sleep, etc., which it is necessary to take into account. These conditions, which are of a perfectly normal character, may produce changes in the temperature amounting to from one to three degrees. It has been ascertained that there are two well-marked periods in the day when the heat is at its maximum. These, according to the most recent observations in Germany, are at eleven A. M. and four P. M.; and it is a curious fact, that while all

[1] W. F. Edwards noted a temperature in the axilla, of a little less than 90°, two or three hours after birth, in an infant born at the seventh month (*Op. cit.*, p. 236).

[2] See vol. i., Respiration, p. 420, *et seq.*

[3] DAVY, *On the Temperature of Man in advanced Age.—Physiological Researches*, London, 1863, p. 4, *et seq.*

observations agree upon this point, the very elaborate experiments of Lichtenfels and Fröhlich show that these periods are well-marked, even when no food is taken. Bärensprung and Ladame further show that the fall in temperature during the night takes place sleeping or waking; and that when sleep is taken during the day it does not disturb the period of the maximum, which occurs at about four P. M.[1]

According to these experiments, at eleven in the morning, the animal heat is at one of its periods of maximum; it gradually diminishes for two or three hours and is raised again to the maximum at about four in the afternoon, when it again undergoes diminution until the next morning. The variations amount to from about 1° to 2·16.° The minimum is always during the night.

The relations of the animal temperature to digestion are still somewhat indefinite. It is well known that activity of the digestive organs increases the consumption of oxygen, and, to a corresponding degree, the exhalation of carbonic acid; but we have to assume that the production of heat is in direct ratio to the respiratory action in order to establish any relation between calorification and the digestion of ordinary food. It is easy to calculate that a given amount of oxygen will produce a definite quantity of carbonic acid, and will, by its union with carbon and hydrogen, generate a certain number of "units of caloric;" but the mechanism of the production of animal heat is too complex and not well enough understood to admit of such positive reasoning. There is, indeed, no experimental evidence of any marked and constant change in the general temperature of the body during the ordinary process of digestion; but it is none the less true that the quantity and quality of food bear

[1] LICHTENFELS UND FRÖHLICH, *Beobachtungen über die Gesetze des Ganges der Pulsfrequenz und Körperwärme in den normalen Zuständen.—Denkschriften der kaiserlichen Akad. der Wissenschaften, mathematisch-naturwissenschaftliche Classe*, Wien, 1852, Bd. iii., Zweite Abth., S. 113, *et seq.*

[2] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., pp. 499, 534.

a certain relation to calorification. This is inevitable from the connection of animal heat with the general process of nutrition; but this relation is expressed in the connection of calorification with nutrition of the tissues, and not in the process of preparation or absorption of food. We shall see that when nutrition is modified by alimentation, the general temperature is always more or less affected; and when the requirements of the system, as far as the generation of heat is concerned, are changed, by climate or otherwise, alimentation is modified. One of the objects of alimentation and nutrition is to maintain the body at a nearly constant temperature.

The influence of defective nutrition or inanition upon the heat of the body is very marked. John Hunter, in his experiments upon animal heat, made a few observations upon this point, and noted a decided fall in temperature in a mouse kept fasting.[1] The same phenomena were also observed by Collard de Martigny;[2] but Chossat, to whose memoir we have so fully referred in another volume under the head of inanition, noted the effects of deprivation of food upon the power of maintaining the animal temperature, in the most exact and satisfactory manner. This point has already been so fully considered that it is only necessary in this connection to note the general results. In pigeons, the extreme diurnal variation in temperature, under normal conditions, was found by Chossat to be 1·3.° During the progress of inanition, the daily variation was increased to 5·9,° with a slight, but well-marked diminution in the absolute temperature; and the periods of minimum temperature were unusually prolonged. Immediately preceding death from starvation, the diminution in temperature became very rapid, the rate, in the observations on turtle-doves, being

[1] *Op. cit.*, p. 114.

[2] Collard de Martigny, *Recherches expérimentales sur les effets de l'abstinence complète d'alimens solides et liquides.—Journal de physiologie*, Paris, 1828, tome viii., p. 163.

from 7° to 11° per hour. Death usually occured when the diminution had amounted to about 30°.[1]

When the surrounding conditions call for the development of an unusual amount of heat, the diet is always modified, both as regards the quantity and kind of food; but when food is taken in sufficient quantity and is of a kind capable of maintaining proper nutrition, its composition does not affect the general temperature. If we were to adopt without reserve the view that the non-nitrogenized alimentary principles are the sole agents in the production of heat, we should certainly be able to determine either an increase in the animal heat or a greater loss of heat from the surface, in persons partaking largely of this kind of food. This, however, has not been shown to be true; and the temperature of the body seems to be uniform in the same climate, even in persons living upon entirely different kinds of food. The elaborate observations of Dr. Davy are very conclusive on this point: "The similarity of temperature in different races of men is the more remarkable, since between several of them whose temperatures agreed, there was nothing in common but the air they breathed—some feeding on animal food almost entirely, as the Vaida—others chiefly on vegetable diet, as the priests of Boodho—and others, as Europeans and Africans, on neither exclusively, but on a mixture of both."[2]

Nevertheless, the conditions of external temperature have a remarkable influence upon the diet. It is well known, for example, that in the heat of summer, the amount of meats and fat taken is small, and the succulent, fresh vegetables and fruits, large, as compared with the diet in the winter. But although the proportion of starchy matters in many of the fresh vegetables used during a short season of the year is not large, these articles are equally deficient

[1] CHOSSAT, *Recherches expérimentales sur l'inanition*, Paris, 1843, p. 123.

[2] DAVY, *Researches, Physiological and Anatomical*, London, 1839, vol. i., p. 197.

in nitrogenized matter. During the winter, the ordinary diet, composed of meat, fat, bread, potatoes, etc., contains a large amount of nitrogenized substance, as well as a considerable proportion of the hydro-carbons; and in the summer, we instinctively reduce the proportion of both of these varieties of principles, the more succulent articles taking their place. This is even more strikingly illustrated by a comparison of the diet in the torrid or temperate and the frigid zone. Under the head of alimentation, we have already noted the prodigious quantities of food consumed in the Arctic regions, and the effect of the continued cold upon the habits of diet of persons accustomed to a temperate climate. It is stated, on undoubted authority, that the daily ration of the Esquimaux is from twelve to fifteen pounds of meat, about one-third of which is fat. Dr. Hayes, the Arctic explorer, noted that with a temperature ranging from —60° to —70,° there was a continual craving for a strong, animal diet, particularly fatty substances. Some of the members of the party were in the habit of drinking the contents of the oil-kettle with evident relish.[1]

Under such conditions as those which surround inhabitants of temperate regions, in passing into the frigid zones a change in diet is imperatively demanded, in order to keep the animal temperature at the proper standard; but when the climate is changed from the temperate to the torrid, the habits of life frequently remain the same. It is a pretty general opinion among physicians who have studied the subject specially, that many of the peculiar disorders that affect those who have changed their residence from a temperate to a very warm climate are due, in a great measure, to the fact that the diet and habits of life are unchanged.

The influence of alcoholic beverages upon the animal temperature has been studied chiefly with reference to the

[1] HAYES, *An Arctic Boat-Journey*, Boston, 1860, pp. 257, 259, and *American Journal of the Medical Sciences*, Philadelphia, 1859, New Series, vol. xxxviii., p. 114, *et seq.*

question of their use in enabling the system to resist excessive cold. Davy states that "the effect of wine, unless used in great moderation, is commonly lowering, that is, as to temperature, while it accelerates the heart's action, followed after a while by an increase of temperature."[1] We have already discussed somewhat fully the physiological effects of alcohol, and have shown that its use does not enable men to endure a very low temperature for a great length of time. This is the universal testimony of scientific Arctic explorers; and Dr. Hayes particularly states, that "in almost any shape, it is not only completely useless, but positively injurious."[2]

The relations of animal heat to respiration and nutrition constitute a most interesting and important division of the subject, which will be more fully considered in discussing the various theories of calorification. As a rule, when the respiratory activity is physiologically increased, as it is by exercise, bodily or mental, ingestion of food, or diminished external temperature, the generation of heat in the body is correspondingly augmented; and, on the other hand, it is diminished by conditions which physiologically decrease the absorption of oxygen and the exhalation of carbonic acid. The only positive experiments upon the influence of simple increase in the number and extent of the respiratory acts are those of Prof. Lombard. He found that when the respirations were increased in depth and frequency for ten minutes, there was a diminution of two degrees in the temperature over the radial artery. There was also a very slight lowering of the temperature, from ·001 to ·01 of a degree cent., in from a minute to a minute and a half after suspension of respiration. Prof. Lombard explains these phenomena by the mechanical effects of the condition of the lungs upon the arterial pressure.[3]

[1] DAVY, *Physiological Researches*, London, 1863, p. 57.

[2] HAYES, *Observations on the Relations existing between Food and the Capabilities of Men to resist Low Temperatures.—American Journal of the Medical Sciences*, Philadelphia, 1859, New Series, vol. xxxviii., p. 117.

[3] LOMBARD, *Recherches expérimentales sur quelques influences non étudiées*

The relations of animal heat to the general process of nutrition are most intimate. Any condition that increases the activity of nutrition and of disassimilation, or even anything that increases disassimilation alone, will increase the production of heat. The reverse of this proposition is equally true. In pathology, the heat of the body may be increased by a deficient action of the skin in keeping down the temperature, without any increase in the activity of calorification.

Influence of Exercise, etc., upon the Heat of the Body.—The influence of muscular activity upon animal heat is peculiarly interesting in connection with the theories of calorification, from the fact that the muscular system constitutes the greatest part of the organism; and, as has repeatedly been shown by experiment, a muscle taken from a living animal is not only capable of contraction upon the application of a stimulus, but will perform for a time certain of the acts of nutrition and disassimilation, such as the appropriation of oxygen and the generation and exhalation of carbonic acid.

The most complete repose of the muscular system is observed during sleep, when hardly any of the muscles are brought into action, except those concerned in tranquil respiration. There is always a notable diminution in the general temperature at this time. John Hunter found a difference, in man, of about one degree and a half.[1] This fact has been confirmed by all who have studied the question experimentally. In the diurnal variations in the temperature of the body, the minimum is always during the night; and, as we have already seen, this is not entirely dependent upon sleep, for a depression in temperature is constantly observed at that time, even when sleep is avoided.[2]

It is a matter of common observation, that one of the

jusqu'ici de la respiration sur la température du corps humain.—Archives de physiologie, Paris, 1868, tome i., p. 496.

[1] HUNTER, *Observations on certain Parts of the Animal Œconomy*, London, 1792, p. 114.

[2] See p. 407.

most effective methods of resisting the depressing influence of cold is to constantly exercise the muscles; and it is well known, that after long exposure to intense cold, the tendency to sleep, which becomes almost irresistible, if indulged in, is followed by a very rapid loss of heat and almost certain death. It is not necessary to cite the accounts of travellers and others in support of these facts. In some animals, the amount of increase in the temperature during muscular activity is very great, and this is notably marked in the class of insects. In the experiments of Newport, on bees and other insects, a difference of about 27° was noted between the conditions of complete repose and great muscular activity.[1] The same facts were observed by Dutrochet, but he operated upon single insects, and observed an elevation of only a fraction of a degree.[2] These facts are interesting, as showing the very great elevation of temperature that can be produced in the lower order of beings during violent excitement; but in man, the differences, though distinct, are never very considerable, for the reason that violent muscular exertion is generally attended with greatly-increased action of the skin, which keeps the heat of the body within very restricted limits. In the experiments of Newport, the loss of heat from the surface was arrested by confining the insects in small glass bottles.

The effects of active exercise, as in fast walking or riding, were very well observed by Dr. Davy. He found a constant elevation in the general temperature (taken under the tongue), amounting to between one and two degrees;[3] but the most marked effects were observed in the extremities, especially when they were cold before taking the exercise.[4]

[1] NEWPORT, *On the Temperature of Insects, and its Connexion with the Functions of Respiration and Circulation in this Class of Invertebrate Animals*—*Philosophical Transactions*, London, 1837, p. 281.

[2] DUTROCHET, *Recherches sur la chaleur propre des êtres vivans à basse température*.—*Annales des sciences naturelles*, *Zoologie*, Paris, 1840, 2me série, tome xiii., p. 48, *et seq.*

[3] DAVY, *Physiological Researches*, London, 1863, p. 16. [4] Ibid., p. 11.

The elevation in temperature that attends muscular action is produced directly in the substance of the muscle. This important fact was settled by the very interesting and ingenious experiments of Becquerel and Breschet. Introducing a thermo-electric needle into the biceps of a man who used the arm in sawing wood for five minutes, these physiologists noted an elevation of temperature of one degree centigrade[1] (nearly two degrees Fahr.). The production of heat in the muscular tissue was even more strikingly illustrated by Matteucci, in experiments with portions of muscle from the frog. Not only did he observe absorption of oxygen and exhalation of carbonic acid and water after the muscle had been removed from the body of the animal, but he noted an elevation in temperature of about one degree Fahr., following contractions artificially excited.[2]

It is useless to multiply citations of experiments illustrating the facts above noted, or to discuss elaborately the theoretical transformation of a given quantity of caloric into a definite and invariable amount of work. The conditions in the animal economy are such that we cannot exactly appreciate the loss of heat by the cutaneous and respiratory surfaces; nor can we follow the processes in the body which involve the disappearance of oxygen and the evolution of carbonic acid; the exact changes undergone by the hydrocarbonaceous elements of food and constituents of the body; the amount of heat involved in the changes of the nitrogenized elements; and, in short, we cannot make the corrections that are absolutely necessary before we can hope to reduce the question of the oxidation of certain principles in the body, the development of heat, and the generation of mechanical force, to exact mathematical calculation. This has been attempted by Béclard[3] and others, who have endeavored to

[1] BECQUEREL ET BRESCHET, *Premier mémoire sur la chaleur animale.—Annales de chimie et de physique*, Paris, 1835, tome lix., p. 113.

[2] MATTEUCCI, *Recherches sur les phénomènes physiques et chimiques de la contraction musculaire.—Comptes rendus*, Paris, 1856, tome xlii., p. 651.

[3] BÉCLARD, *De la contraction musculaire dans ses rapports avec la température*

establish the numerical value of certain acts in what are called "mechanical equivalents of heat," or "heat-units." The observations of Béclard possess considerable physiological interest, but they are useful chiefly, if not entirely, in their positive results.

Observations upon the influence of mental exertion on the temperature of the body have not been so numerous, but they are, apparently, no less exact in their results. Dr. Davy was the first to make any extended experiments on this point, and has noted a slight but constant elevation during "excited and sustained attention."[1] More lately, the same line of observation has been followed by Prof. Lombard, who employed much more exact methods of investigation. Prof. Lombard noted an elevation of temperature in the head during mental exertion of various kinds, but it was slight, the highest rise not exceeding the twentieth of a degree.[2]

It is stated, also, that the temperature of the body is increased by the emotions of hope, joy, anger, and all exciting passions; while it is diminished by fear, fright, and mental distress. Burdach, from whom the foregoing statement is taken, cites an example of an elevation of temperature from 96° to 99·5° in a violent access of anger, and a descent to 92·75° under the influence of fear, but the temperature soon returned to 97·25°.[3]

The nervous system exerts a most important influence over the animal temperature, as it modifies the circulation and the nutritive processes in particular parts. The most interesting of these influences are transmitted through the sympathetic system. These will be discussed, to a certain extent, in connection with the theories of calorification; but they cannot be taken up fully until we come to consider the

animale.—Archives générales de médecine, Paris, 1861, 5me série, tome xvii. The conclusions in this interesting memoir are to be found on page 277, *et seq.*

[1] DAVY, *Physiological Researches*, London, 1863, pp. 19, 51.

[2] LOMBARD, *Experiments on the Relations of Heat to Mental Work.—New York Medical Journal*, 1867, vol. v., p. 198, *et seq.*

[3] BURDACH, *Traité de physiologie*, Paris, 1841, tome ix., p. 645.

functions of the sympathetic system and its relations to nutrition. In this connection, we shall simply allude to certain phenomena manifested through the nervous system, without attempting to fully explain their mechanism.

It is well known that when the sympathetic nerves going to a particular part are divided, the arterial coats are paralyzed and dilated, the supply of blood is increased, nutrition is locally exaggerated and more or less modified, and the temperature of that particular part is increased by from five to ten degrees. An illustration of these facts in the ear of the rabbit, after division of the sympathetic in the neck, is a very common observation, which we have often verified in public demonstrations. All of these unnatural phenomena disappear on galvanizing the divided extremity of the nerve. These local modifications in the temperature have been frequently observed pathologically in the human subject.

A number of curious local variations of temperature can be explained by direct or reflex action through the sympathetic nerves. Brown-Séquard and Lombard observed that pinching of the skin was soon followed by an elevation in temperature, and was attended also with a diminution in the temperature in the corresponding member on the opposite side. Sometimes the irritation of the upper extremities produced changes in temperature in the lower limbs.[1] Examples of reflex action through the sympathetic nerves are given by Tholozan and Brown-Séquard, in a very interesting series of experiments. These physiologists found that lowering the temperature of one hand produced a considerable diminution in the temperature of the other hand, without any great depression in the general heat of the body; and Brown-Séquard showed that by immersing one foot in water at 41°, the temperature of the other foot was diminished about 7° in the course of eight minutes.[2]

[1] BROWN-SÉQUARD ET LOMBARD, *Expériences sur l'influence de l'irritation des nerfs de la peau sur la température des membres.—Archives de physiologie*, Paris, 1868, tome i., p. 691.

[2] THOLOZAN ET BROWN-SÉQUARD, *Recherches expérimentales sur quelqu'uns*

The influence of the cerebro-spinal system upon the animal temperature is illustrated in cases of paralysis, when there is generally a very considerable diminution in the heat of the affected part. This fact was noted, many years ago, by Earle, who also observed that the temperature was in part restored under the influence of electricity. In one case of paralysis, he found the temperature of the hand of the affected side 70°, while the hand of the sound side was 92°. After the use of electricity for ten minutes, the temperature of the paralyzed hand was raised to 74°. Ten days after, the temperature of the hand on the paralyzed side was 71° before, and 77° after electricity had been employed.[1]

It is evident that if animal heat be one of the necessary attendant phenomena of nutrition, it must be greatly influenced by the state of the circulation. It has been a question, indeed, whether the modifications in temperature produced by operating upon the sympathetic system of nerves be not due entirely to changes in the supply of blood. It is certain that whatever determines an increased supply of blood to any part raises the temperature; and whenever the quantity of blood in any organ or part is considerably diminished, the temperature is reduced. This fact is constantly illustrated in operations for the deligation of large arteries. It is well known that after tying a large vessel, the utmost care is necessary to keep up the temperature of the part to which its branches are distributed, until the anastomosing vessels become enlarged sufficiently to supply blood enough for healthy nutrition. In the experiments of Becquerel and Breschet, simple compression of the artery supplying the arm was sufficient to produce an immediate fall in the temperature.[2]

Effets du froid sur l'homme.—Journal de la physiologie, Paris, 1858, tome i., pp. 502, 505.

[1] EARLE, *Cases and Observations, illustrating the Influence of the Nervous System in regulating Animal Heat.—Medico-Chirurgical Transactions*, London, 1816, vol. vii., p. 176.

[2] *Loc. cit.*

CHAPTER XIV.

SOURCES OF ANIMAL HEAT.

Connection of the production of heat with nutrition—Seat of the production of animal heat—Relations of animal heat to the different processes of nutrition—Relations of animal heat to respiration—The consumption of oxygen and the production of carbonic acid in connection with the evolution of heat—Exaggeration of the animal temperature in particular parts after division of the sympathetic nerve and in inflammation—Intimate nature of the calorific processes—Equalization of the animal temperature.

THE most interesting question connected with calorification relates to the sources of heat in the living organism; and a careful estimate of the physiological value of all the facts that have been positively established with reference to this point places the following proposition beyond any reasonable doubt:

The generation of heat in the living animal organism is connected, more or less intimately, with all of the processes of nutrition and disassimilation, including, of course, the consumption of oxygen and the production of carbonic acid; and this function is modified, to a greater or less degree, by all conditions that influence the general process of nutrition or the operation of the nutritive forces in particular parts.

This proposition is not contradicted by any well-settled physiological facts or principles. Every one of the functions of the body bears more or less closely upon nutrition; and all of the physiological modifications of the various functions, without exception, affect the process of calorification. We must bear in mind the fact, that in man and the warm-

blooded animals generally, the maintenance of the temperature of the organism at a nearly fixed standard is a necessity of life and of the physiological action of the different parts; and that while heat is generated in the organism with an activity that is constantly varying, it is as constantly counterbalanced by physiological loss of heat from the cutaneous and respiratory surfaces. Variations in the activity of calorification are not to be measured by corresponding changes in the temperature of the body, but are to be estimated by calculating the amount of heat lost. The ability of the human race to live in all climates is explained by the adaptability of man to different conditions of diet and exercise, and to the power of regulating loss of heat from the surface by appropriate clothing.

Our proposition regarding the production of animal heat is in no wise opposed to the so-called combustion-theory, as it is received by most physiologists of the present day; but it must be admitted that it is an unfortunate use of terms to apply the name combustion to the general process of nutrition, as is done by those who attempt to preserve, not only the ideas of the great author of this theory, but certain modes of expression, which were in accordance only with his limited knowledge of the phenomena of nutrition. If we speak of animal heat as the result of combustion of certain elements, it will be necessary constantly to refer to the difference between combustion as it occurs in the organism, and mere oxidation out of the body; or to start with a full definition of what is to be understood by the term physiological combustion, which reduces itself simply to a definition of nutrition.

Regarding calorification, then, as connected with all of the varied processes of nutrition, it remains for us to determine the following questions:

1. In what part or parts of the organism is heat generated?

2. What is the relative importance in calorification, as

regards the amount of heat generated, of the processes nutrition, as we can study them separately?

3. What are the principles invariably and of necessity consumed and produced in the organism in calorification and what is the relative importance of the principles thus consumed and the products thus generated and thrown off?

4. How far have we been able to follow those material transformations in the organism, which involve the consumption of certain principles, the production of new compounds, and the generation of heat?

Seat of the Production of Animal Heat.—Few if any physiologists at the present day hold to the opinion that there is any part or organ in the body specially and exclusively concerned in the production of heat. In the early history of the oxidation-theory of Lavoisier, it was thought by some that the inspired oxygen combined with the hydrocarbons of the blood in the lungs, and that the heat of the body was generated almost exclusively in these organs; but this idea has long since been abandoned. We have already fully considered the question of loss or gain in the temperature of the blood in its passage through the lungs, and have seen that there is, to say the least, no constant elevation showing a generation of heat in these organs, sufficient to warm the blood, and through it the different parts of the body. If we find that the blood in coming from the lungs has about the same temperature as when it entered, it must be admitted that there is a certain generation of heat to compensate the loss by evaporation from the pulmonary surface. As far as we know, the heat that results from the mere physical solution of oxygen in the blood is all that is produced in the lungs. It is, indeed, estimated by Marchand, that the fixation of oxygen in this way is marked by an elevation of nearly 2° Fahr.[1] There is no sufficient evi-

[1] MARCHAND, *Ueber die Einwirkung des Sauerstoffs auf das Blut und seine Bestandtheile.*—*Journal für praktische Chemie*, Leipzig, 1845, Bd. xxxv., S. 400.

dence to show that the lungs are special organs of calorification; and any generation of heat that takes place here is due, probably, to purely physical phenomena in the blood.

The theory that all the respiratory changes, involving the consumption of oxygen, the production of carbonic acid, and the evolution of heat, take place in the blood as it circulates, was advanced many years ago by Lagrange and Hassenfratz;[1] but recent investigations, showing the appropriation of oxygen and the evolution of carbonic acid by the tissues deprived of blood, and the evident production of heat in the muscular substance and in other parts, have completely overthrown this hypothesis.

It is only necessary to refer back to the pages treating of the variations in the temperature of the blood in different parts, to show that heat is produced in the general system, and not in any particular organ, or in the blood as it circulates. The experiments of Matteucci, showing an elevation of temperature in a muscle excited to contraction after it had been removed from the body, and the observations of Becquerel and Breschet, showing increased development of heat by muscular contraction, are sufficient evidence of the production of heat in the muscular system;[2] and, inasmuch as this constitutes by far the greatest part of the weight of the body, it is a most important source of animal heat.

It has been demonstrated, by the experiments of Bernard, that the blood becomes notably warmer in passing through the abdominal viscera. This is particularly marked in the liver, and it shows that the large and highly-organized viscera are also important sources of caloric.[3]

As far as it is possible to determine by experimental demonstration, not only is there no particular part or organ

[1] HASSENFRATZ, *Mémoire sur la combinaison de l'oxygène avec le carbone et l'hydrogène du sang, sur la dissolution de l'oxygène dans le sang, et sur la manière dont le calorique se dégage.*—*Annales de chimie*, Paris, 1791, tome ix., p. 261.

[2] See page 414.

[3] See page 399.

in the body endowed with the special function of calorification, but every part in which the nutritive forces are in operation produces a certain amount of heat; and this is probably true of the blood-corpuscles and other anatomical elements of this class. The production of heat in the body is general, and is one of the necessary consequences of the process of nutrition; but, with nutrition, it is subject to local variations, as is strikingly illustrated in the effects of operations upon the sympathetic system of nerves, and the phenomena of inflammation.

Relations of Animal Heat to the different Processes of Nutrition.—Nutrition involves the appropriation of matters taken into the body, and the production and elimination of effete substances. In its widest signification, this includes the consumption of oxygen and the elimination of carbonic acid; and, consequently, we may strictly regard respiration as a nutritive act. All of the nutritive processes go on together, and they all involve, in most warm-blooded animals at least, a nearly uniform temperature. During the first periods of embryonic life, the heat derived from the mother is undoubtedly necessary to the development of tissue by a change of substance, analogous to nutrition, and even superior to it in activity. During adult life, animal heat and the nutritive force are coexistent. It now becomes a question to determine whether there be any class of nutritive principles specially concerned in calorification, or any of the nutritive acts, that we have been able to study by themselves, which are exclusively or specially directed to the maintenance of the temperature of the body. These questions simply involve a review of considerations with regard to the relations of various of the functions to the production of heat.

The supply of the waste of tissue being effected by metamorphosis of alimentary matter—a process, the exact nature of which we have not been able to determine—it has thus

far been possible, only, to divide the food into different classes. Of these, leaving out oxygen, we shall consider, in this connection, the organic matters, divided into nitrogenized and non-nitrogenized. The inorganic salts are always combined with nitrogenized matter, and seem to pass through the organism without undergoing any considerable change; and there is no evidence that they have any connection, of themselves, with the production of heat.

What is the relation to calorification of those processes of nutrition which involve the consumption of nitrogenized matter and the production of the nitrogenized excrementitious principles?

We cannot study these phenomena alone, isolated from the other acts of nutrition. We may confine an animal to a purely nitrogenized diet, and the heat of the body will be maintained at the proper standard; but at all times there is a certain quantity of non-nitrogenized matter (sugar and perhaps fat) produced in the system, which is only formed to be consumed. We may starve an animal, and the temperature will not fall to any very great extent until a short time before death. Here we may suppose that the process of deposition of nutritive matter in the tissues from the blood is inconsiderable, as compared with the transformation of the substance of these tissues into effete matter; and it is almost certain that non-nitrogenized matter is not produced in the organism in quantity sufficient to account, by its destruction in the lungs, for the carbonic acid exhaled. It seems beyond question that there must be heat evolved in the body by oxidation of nitrogenized matter. When the daily amount of food is largely increased for the purpose of generating the immense amount of heat required in excessively cold climates, the nitrogenized matters are taken in greater quantity, as well as the fats, although their increase is not in the same proportion. When, however, we endeavor to assign to the nitrogenized matters a definite proportion of heat-producing power, we are arrested by a want of positive knowl-

edge with regard to the metamorphoses which these principles undergo; and it is equally impossible to fix the relative calorific value of the deposition of new material in repair of the tissues, and the change of their substance into effete matter in disassimilation.

From these facts, and other considerations that have already been fully discussed under different heads, it is evident that the physiological metamorphoses of nitrogenized matter bear a certain share in the production of animal heat; although, in connection with inorganic matter, their chief function seems to be the repair of the tissues endowed with the so-called vital properties.

What is the relation of the consumption of non-nitrogenized matter to the production of animal heat?

It has been impossible to treat of the relations of the non-nitrogenized elements to nutrition without considering more or less fully the part these principles bear in the production of heat; and we must refer the reader to the previous chapter for a discussion of certain of these points.[1] In this connection, we shall simply state the relations that this class of principles is known to bear to calorification, and the facts upon which our statements are based.

It has been pretty clearly shown that both sugar and fat are actually produced in the organism, even when the diet is strictly nitrogenized in its character; but we shall only consider the relations of the non-nitrogenized elements introduced into the body, assuming that the principles of this class appearing *de novo* in the organism are the result of transformation of nitrogenized substances.

As far as the destination of the amylaceous, saccharine, and fatty elements of food are concerned, we only know that they are incapable, of themselves, of repairing muscular tissue, and that they cannot sustain life. They are never discharged from the body in health in the form under which they enter; but are in part or completely destroyed in nutri-

[1] See page 378, *et seq.*

tion. They are completely destroyed in persons who, from habitual muscular exercise, have very little adipose tissue. When their quantity in the food is large, they are not of necessity entirely consumed, but may be deposited in the form of adipose tissue. This, however, may be made to disappear by violent exercise, or under an insufficient diet.

There can be no doubt that the non-nitrogenized class of alimentary principles is craved by the system in long-continued exposure to extreme cold. This is particularly marked with regard to the fats. In all cold climates, fat is a most imimportant element of food; and in excessively cold regions, while the nitrogenized elements are largely increased, there is a very much larger proportional increase in the quantity of fat. These facts are very significant. If the non-nitrogenized elements of food—which are not always indispensable, though often very necessary articles—do not form tissue, are not discharged from the body, and are consumed in some of the processes of nutrition, it would seem that their change must involve the production of carbonic acid, perhaps also of water, and the evolution of heat. It is so difficult to ascertain the exact quantities of carbonic acid, watery vapor, etc., thrown off by the lungs, skin, and other emunctories, and to estimate the exact amount of heat produced and lost, that it is not surprising that calculations of the calorific power of different articles of food should be frequently erroneous; particularly as we have no means of knowing the exact calorific value of the nitrogenized principles.

Though we may assume that the non-nitrogenized elements of food are particularly important in the production of animal heat, and that they are not concerned in the repair of tissue, it must be remembered that the animal temperature may be kept at the proper standard upon an exclusively nitrogenized diet; and we cannot, indeed, connect calorification exclusively with the consumption of any single class of principles, nor with any single one of the acts of nutrition.

Relations of Calorification to Respiration.—Respiration is one of the nutritive processes that can be closely studied by itself, as it involves the appropriation by the system of a single principle (oxygen), and that simply in solution in the blood. There can be no doubt that, of all the nutritive acts, respiration is, far more than any other, intimately connected with calorification. As far as the general process is concerned, the production of heat is usually in direct ratio to the consumption of oxygen and the exhalation of carbonic acid. In the animal scale, wherever we have the largest amount of heat produced, we observe the greatest respiratory activity. In man, whatever increases the generation of heat increases as well the consumption of oxygen and the elimination of carbonic acid. The production of heat in warm-blooded animals is constant, and cannot be interrupted, even for a few minutes. The same is true of respiration. The tissues may waste for want of nourishment, but the heat of the body must be kept near a certain standard, which is almost always much higher than the surrounding temperature; and there is no other nutritive act so constant and so immediately necessary to existence as the appropriation of oxygen. It is not surprising, then, that early in the history of the physiology of nutrition, before we knew, even, the exact condition and proportion of the gases in the blood, it should have been thought that animal heat was the result of slow combustion of the hydro-carbons.

The physiological history of respiration and of animal heat dates from the same series of discoveries. In the latter part of the last century, the great chemist, Lavoisier, discovered the intimate nature of the respiratory process, and applied the theory of the consumption of oxygen and the evolution of carbonic acid to calorification. We have already followed out the progress of this discovery in connection with respiration;[1] and like nearly all of the great advances in physiological science, the distinctly-enunciated idea was foreshadowed

[1] See vol. i., Respiration, p. 409, *et seq.*

by earlier writers. The most remarkable of these was Mayow, who, in 1667, and afterward in 1674, published a work on the *Spiritus Nitro-aëreus*, and on respiration, in which he attributed to the nitro-aëreous gas (oxygen) the property of combining with the blood in the lungs, producing the red color, and generating heat.[1] These ideas, as well as those advanced by Crawford, near the time of the publication of the first observations of Lavoisier, were crude and indefinite, and contributed but little to our positive knowledge of the mechanism of calorification.[2]

It will not be necessary to treat, from a purely historical point of view, of the discoveries made by Lavoisier, as this has already been done sufficiently under the head of respiration.[3] He undoubtedly went as far in his explanations of the phenomena of animal heat as was possible in the condition of the science at the time his investigations were made; and although he inevitably fell into some errors in his calculations and deductions, he must forever be regarded as the author of the first reasonable theory of the generation of heat by animals.

The Consumption of Oxygen and Production of Carbonic Acid in Connection with the Evolution of Heat.—As far as it has been possible to determine by actual experiment,

[1] MAYOW, *Tractatus quinque Medico-physici. Quorum primus agit de Salnitro, et Spiritu Nitro-aëreo. Secundus de Respiratione, etc.*, Oxonii, 1674, p. 151, *et seq.* The first edition of the work on Respiration was published in 1767.

[2] CRAWFORD, *Experiments and Observations on Animal Heat*, London, 1788, second edition, p. 354, *et seq.* Crawford published the first edition of his work in 1779, but the second edition, in which his views are avowedly made to correspond with the observations of Lavoisier, is the only one at all accessible. From all we can learn of the matter contained in the first edition, from extracts and references in other treatises, Crawford's ideas were not in advance of those presented by Lavoisier to the Academy of Sciences, in 1777.

[3] The various papers published by Lavoisier and Seguin, and Lavoisier and de la Place, are scattered through the volumes of memoirs of the French Academy of Sciences, from 1777 to 1790. An exhaustive analytical review of these memoirs is given by Gavarret (*De la chaleur produite par les êtres vivants*, Paris, 1855, p. 165, *et seq.*).

all animals, even those lowest in the scale, appropriate oxygen and eliminate carbonic acid; and this is equally true of all living tissues. In 1775, Lavoisier noted the fact that the gas obtained by decomposing the oxide of mercury was more active than the air in maintaining the respiration of animals.[1] Two years later, he compared oxidation by respiration in animals to ordinary combustion, and advanced the hypothesis that this action was the cause of the constant temperature of animals of about 32½° Réaumur.[2] A little later, he published the remarkable experiments in which he estimated the amount of "combustion" in a Guinea-pig, by collecting the carbonic acid exhaled, and compared it with the amount of heat lost by the same animal in a definite time.[3] Here he met with some difficulty, and found that the heat produced, according to his calculations, did not quite equal the heat lost. In later memoirs he ascertained positively that the carbonic acid exhaled in respiration did not represent the totality of the oxygen consumed; and he attributed the production of heat in part to the union of oxygen with hydrogen.[4] Since it has been ascertained that oxygen is dissolved, as oxygen, in the arterial blood, that it disappears in part or entirely in the capillary circulation, that carbonic acid is taken up by the venous blood, both in solution and in feeble combination in the bicarbonates, to be discharged in the lungs by displacement and the action of the pneumic

[1] LAVOISIER, *Mémoire sur la nature du principe qui se combine avec les métaux pendant leur calcination, et qui en augmente le poids.—Histoire de l'académie royale des sciences*, année, 1775, Paris, 1778, pp. 521, 525.

[2] LAVOISIER, *Mémoire sur la combustion en général.—Histoire de l'académie royale des sciences*, année, 1777, Paris, 1780, p. 599.

[3] LAVOISIER ET DE LA PLACE, *Mémoire de la chaleur.—Histoire de l'académie royale des sciences*, année, 1780, Paris, 1784, p. 407.

[4] LAVOISIER, *Mémoire sur les altérations qui arrivent à l'air dans plusieurs circonstances où se trouvent les hommes réunis en société.—Histoire de la société royale de médecine*, années, 1782 et 1783, Paris, 1787, p. 574.

SEGUIN ET LAVOISIER, *Premier mémoire sur la respiration des animaux.—Histoire de l'académie royale des sciences*, année, 1789, Paris, 1793, p. 566 *et seq.*

acid, and that the tissues themselves have the property of appropriating oxygen and exhaling carbonic acid, those who adopt the theory of Lavoisier have simply changed the seat of oxidation from the lungs to the general system.

It has been proven beyond question that oxygen, of all the principles introduced from without, is the one most immediately necessary to nutrition; and it differs from the class of substances ordinarily known as alimentary, only in the fact that it is consumed more promptly and constantly. In the same way, carbonic acid is to be regarded as an element of excretion, like urea, creatine, etc., differing from them only in the immediate necessity for its elimination.[1] As the comparatively slow excretion of urea and other nitrogenized matters is connected with the ingestion of ordinary alimentary substances that are slowly appropriated by the tissues, so the rapid elimination of carbonic acid is connected with the equally rapid appropriation of oxygen. There is no reason why we should not regard carbonic acid, like other effete substances, as an excretion, the result of disassimilation of the tissues generally; but, more closely than any, it is connected with the rapid and constant evolution of heat. This view is proven by the experiments of Spallanzani,[2] W. F. Edwards,[3] and Collard de Martigny.[4] All of these eminent observers demonstrated, beyond a doubt, that carbonic acid may be formed in the system and exhaled, in animals deprived of oxygen, and that its exhalation will take place from a piece of tissue freshly removed from a

[1] Collard de Martigny, who was one of the most powerful opponents of the combustion-theory of animal heat, concludes the account of his experiments on the production of carbonic acid with the statement that it "is a product of *assimilative decomposition*, *secreted* in the capillaries, and *excreted* by the lungs" (*Journal de physiologie*, Paris, 1830, tome x., p. 161).

[2] Spallanzani, *Mémoires sur la respiration*, Genève, 1803, pp. 86, 343.

[3] Edwards, *De l'influence des agens physiques sur la vie*, Paris, 1824, p. 443, *et seq.*, and p. 455, *et seq.*

[4] Collard de Martigny, *Recherches expérimentales et critiques sur l'absorption et sur l'exhalation respiratoires.—Journal de physiologie*, Paris, 1830, tome x., p. 124.

living animal and placed in an atmosphere of hydrogen or nitrogen.

Experiments on the influence of the sympathetic nerves upon the temperature of particular parts have completed the chain of evidence in favor of the localization of the heat-producing function in the tissues. It is not our purpose to discuss the relations of the sympathetic system to nutrition, deferring this subject until we come to treat specially of the nervous system; but the facts bearing on calorification are briefly as follows:

If the sympathetic nerve be divided in the neck of a rabbit, or any other warm-blooded animal, the side of the head supplied by this nerve will become from five to eight or ten degrees warmer than the opposite side, or than the rest of the body. This observation we have repeatedly verified. The conditions under which this local exaggeration of the animal heat is manifested are, dilatation of the arteries of supply of the part, so that it receives very much more blood than before, and increased activity of the general process of nutrition. It also has been observed, in experiments upon the horse, that the blood coming from the part is red, and contains very much more oxygen than ordinary venous blood.[1]

The recent observations of MM. Estor and Saint-Pierre show that the blood coming from inflamed parts, in which there is a considerable elevation above the normal temperature, is red, and contains from fifty to two hundred and fifty per cent. more oxygen than ordinary venous blood.[2] These facts are regarded as inconsistent with the view that the temperature of parts is due chiefly to oxidation; but when we consider the fact that, in the conditions above mentioned, the actual quantity of blood circulating in these

[1] BERNARD, *Sur la quantité d'oxygène que contient le sang veneux des organes glandulaires, à l'état de fonction et à l'état de repos.*—*Comptes rendus*, Paris, 1858, tome xlvii., p. 398, note.

[2] ESTOR ET SAINT-PIERRE, *Recherches expérimentales sur les causes de la coloration rouge des tissus enflammés.*—*Journal de l'anatomie*, Paris, 1864, tome i., p. 412, and *Du siége des combustions respiratoires.*—Ibid., 1865, tome ii., p. 314.

parts is increased many times, the error in the deduction is palpable enough. It is not sufficient to show that the blood coming from an inflamed tissue, with an abnormally high temperature, contains more oxygen than under ordinary conditions, but it is indispensable to demonstrate that the absolute quantity of oxygen consumed is diminished. For example, if the venous blood should contain double the normal proportion of oxygen, but the quantity coming from the part should be increased threefold, it is evident that the actual consumption of oxygen would be doubled. As an illustration, let us assume that, in one minute, 100 parts of blood, containing 10 parts of oxygen, circulate through a member, losing in its passage 7·5 parts of oxygen, thus leaving a proportion of 2·5 of oxygen for the venous blood; if the part become inflamed, let us suppose that during the same period, 300 parts of blood, with 30 parts of oxygen, pass through, but that the venous blood contains five per cent. of oxygen, or 15 parts. That would show an actual consumption of 15 parts of oxygen in inflammation, against 7·5 under normal nutrition. Estor and Saint-Pierre do not state the amount of increase in the quantity of blood circulating through inflamed tissues, but they admit that, "in inflammation, the vessels are dilated, and the current of blood is more rapid."[1] An increase in the absolute quantity of blood passing through parts after division of the sympathetic nerves distributed to the coats of the blood-vessels has been observed by all who have experimented on the subject; and the increase is probably greater than that which we have assumed in our argument. An additional argument in favor of our interpretation of the experiments of Estor and Saint-Pierre is the fact, noted by them, that the blood from inflamed parts contains more carbonic acid than ordinary venous blood.[2]

Taking into account all the facts bearing upon the question, there can be little doubt, that while the processes of

[1] *Journal de l'anatomie*, Paris, 1865, tome ii., p. 314.

[2] Idem., Paris, 1864, tome i., p. 412.

nutrition and disassimilation, involving changes in the nitrogenized constituents of the blood and the tissues, are not disconnected with calorification, the production of heat by animals is most closely related to the appropriation of oxygen and the formation of carbonic acid.

Intimate Nature of the Calorific Processes.—A comprehension of the intimate nature of the calorific processes involves simply an answer to the question, how far we can follow the material transformations in the organism, which involve the consumption of certain principles, the production of new compounds, and the evolution of heat. As regards the nature of the intermediate processes connecting the disappearance of oxygen with the production of carbonic acid, we can only explain it by reciting the simple facts. Oxygen disappears, carbonic acid is formed, and the carbon is furnished, perhaps by the tissues, perhaps by the blood, probably by both. It is probable that the intermediate changes are more simple and rapid than those which intervene between the appropriation of nitrogenized nutritive matter and the formation of the nitrogenized excretions; but we have never been able to follow either of these processes through all of their different phases. We must be content, in the present condition of our positive knowledge, to regard calorification as one of the attendant phenomena of nutrition; and we have only to study as closely as possible the facts with regard to the disappearance of certain principles and the formation of effete matters, that are always and of necessity associated with the development of heat.

Equalization of the Animal Temperature.—A study of the phenomena of calorification in the human subject has shown that under all conditions of climate the general heat of the body is equalized. Nearly always, the surrounding temperature is below the standard of the body, and there is, of necessity, an active production of caloric. Under all con-

ditions, there is more or less loss of heat by evaporation from the general surface, and when the surrounding atmosphere is very cold, it becomes desirable to reduce this loss to the minimum. This is done by appropriate clothing, which must certainly be regarded as a physiological necessity. The proper kind of clothing, the conducting power of different materials, their porosity, etc., form important questions in practical hygiene, and their full discussion belongs to special treatises. Clothing protects from excessive heat as well as cold. Thin, porous articles moderate the heat of the sun, equalize evaporation, and afford great protection in hot climates. In excessive cold, clothing is of the greatest importance in preventing the escape of heat from the body. When the body is not exposed to currents of air, the garments are chiefly useful as non-conductors, imprisoning many layers of air, warmed by contact with the person. It is farther very important to protect the body from the wind, which increases so greatly the loss of heat by evaporation. It is wonderful, however, how intense a cold may be resisted by healthy men under proper conditions of alimentation and exercise and with the protection of appropriate clothing, as in Arctic explorations, when the thermometer has for days ranged from —60° to —70° Fahr.[1]

When from any cause there is a tendency to undue elevation of the heat of the body, cutaneous transpiration is increased, and the temperature is kept at the proper standard. We have already considered this question in treating of the action of the skin, and have noted facts showing that men can work when exposed to a heat much higher than that of the body itself. The amount of vapor that is lost under these conditions is sometimes enormous, amounting to from two to four pounds in an hour.[2] We have often noted a loss of between two and three pounds after exposure for less

[1] HAYES, *An Arctic Boat-Journey*, Boston, 1860, pp. 257, 259, and *American Journal of the Medical Sciences*, Philadelphia, 1859, New Series, vol. xxxviii., p. 114, *et seq.*

[2] See page 140.

than an hour to a steam-bath of from 110° to 116°; and a much greater elevation of temperature, in dry air, can be tolerated with impunity. We have alluded to some of the observations on the temperatures that could be borne without bad results, in connection with the question of variations in the heat of the body. In the experiments of Delaroche and Berger, the temperature was considerably under 200°.[1] Tillet recorded an instance of a young girl who remained in an oven for ten minutes without inconvenience, at a temperature of 130° Réaumur, or 324·5° Fahr.[2] Dr. Blagden, in his noted experiments in a heated room, made in connection with Drs. Banks, Solander, Fordyce, and others, found in one series of observations, that a temperature of 211° could be easily borne; and at another time, the heat was raised to 260°.[3] Chabert, who exhibited in this country and in Europe under the name of the "fire-king," is said to have entered ovens at from 400° to 600°.[4] Under these extraordinary temperatures, the body is protected from the radiated heat by clothing, the air is perfectly dry, and the animal heat is kept down by excessive exhalation from the surface.

It is a curious fact, that after exposure of the body to an intense dry heat or to a heated vapor, as in the Turkish and Russian baths, when the general temperature is somewhat raised and the surface is bathed in perspiration, a cold plunge, which checks the action of the skin almost immediately, is not injurious, and is rather agreeable. This presents a striking contrast to the effects of sudden cold upon a system, heated and exhausted by long-continued exertion. In the latter instance, when the perspiration is suddenly checked, serious disorders of nutrition, inflammations, etc.,

[1] See page 397.

[2] TILLET, *Mémoire sur les degrés extraordinaires de chaleur auxquelles les hommes et les animaux sont capables de résister.—Histoire de l'académie royale des sciences*, année, 1764, Paris, 1767, p. 188.

[3] BLAGDEN, *Experiments and Observations in an heated Room.—Philosophical Transactions*, London, 1775, pp. 196, 484.

[4] DUNGLISON, *Human Physiology*, Philadelphia, 1856, vol. i., p. 598.

are very liable to occur. The explanation of this, as far as we can present any, seems to be the following: When the skin acts to keep down the temperature of the body in simple exposure to external heat, there is no modification in nutrition, and the tendency to an elevation of the animal temperature comes from causes entirely external. It is a practical observation that no bad effects are produced, under these circumstances, by suddenly changing the external conditions; but when the animal temperature is raised by a modification of the internal nutritive processes, as in prolonged muscular effort, these changes cannot be suddenly arrested; and a suppression of the compensative action of the skin is apt to produce disturbances in nutrition, very often resulting in inflammations.

CHAPTER XV.

MOVEMENTS—GENERAL PROPERTIES OF CONTRACTILE TISSUES.

Amorphous contractile substance—Ciliary movements—Movements due to elasticity—Varieties of elastic tissue—Muscular movements—Physiological anatomy of the involuntary muscles—Mode of contraction of the involuntary muscular tissue—Physiological anatomy of the voluntary muscles—Primitive fasciculi—Sarcolemma—Fibrillæ—Fibrous and adipose tissue in the voluntary muscles—Connective tissue—Blood-vessels and lymphatics of the muscular tissue—Connection of the muscles with the tendons—Chemical composition of the muscles—Physiological properties of the muscles—Elasticity—Muscular tonicity—Sensibility of the muscles—Muscular contractility, or irritability.

THE organic, or vegetative functions of animals involve certain movements; and almost all animals possess, in addition, the power of locomotion. Very many of these movements have, of necessity, been considered in connection with the different functions; as the action of the heart and vessels in the circulation; the uses of the muscles in respiration; the ciliary movement in the air-passages; the muscular acts in deglutition; the peristaltic movements; and the mechanism of defecation and urination. There remain, however, certain general facts with regard to various kinds of movement and the mode of action of the different varieties of muscular tissue, that will demand more or less extended consideration. As regards the exceedingly varied and complex acts concerned in locomotion, it is difficult to fix the limits between anatomy and physiology. A full comprehension of such movements must be preceded by a complete

descriptive anatomical account of the passive and active organs of locomotion; and special treatises on anatomy almost invariably give the uses and actions, as well as the structure and relations of these parts.

Amorphous Contractile Substance.—In some of the very lowest orders of beings, in which hardly any thing but amorphous matter and a few granules can be recognized by the microscope, certain movements of elongation and retraction of their amorphous substance have been observed. In the higher animals, similar movements have been noticed in certain of their structures, such as the leucocytes, the contents of the ovum, epithelial cells, and connective-tissue cells. These movements are generally simple changes in the form of the cell, nucleus, or whatever it may be. They are supposed to depend upon an organic principle called sarcode, or protoplasm;[1] but it is not known that such movements are characteristic of any one definite proximate principle, nor is it easy to determine their cause and their physiological importance. In the anatomical elements of adult animals of the higher classes, the sarcodic movements usually appear slow and gradual, even when viewed with high magnifying powers; but in some of the very lowest orders of being these movements serve as the means of progression, and are more rapid. Such movements are sometimes called amœboid.

It does not seem possible, in the present condition of our knowledge, to explain the nature and cause of the movements of homogeneous contractile substance; and it must be excessively difficult, if not impossible, to observe directly the effects of different stimuli, in the manner in which we study the movements of muscles. As far as we can judge,

[1] KÜHNE, *Untersuchungen über das Protoplasma und die Contractilität*, Leipzig, 1864. In this very elaborate memoir almost all varieties of contraction are referred to the action of the single principle, protoplasm. The chief physiological interest, however, is attached to this explanation of muscular contraction; but there are few writers of authority who accept the view that it is entirely due to the presence of the so-called protoplasm.

they are analogous to the ciliary movements, the cause of which is equally obscure.

Ciliary Movements.—The epithelium covering certain of the mucous membranes is provided with little hair-like processes upon the free portion of the cells, called cilia. These are in constant motion, from the beginning to the end of life, and produce currents on the surfaces of the membranes to which they are attached, the direction being generally from within outward. In many of the infusoria, the ciliary motion serves as a means of progression, effects the introduction of nutriment into the alimentary canal, and, indeed, is almost the sole agent in the performance of the functions involving movement. Even in higher classes, as the mollusca, the movements of the cilia are of great importance. In man, and the warm-blooded animals generally, the ciliated or vibratile epithelium is of the variety called columnar, conoidal, or prismoidal. The cilia are attached to the thick ends of the cells, and form on the surface of the membrane a continuous sheet of vibrating processes.

It is unnecessary to describe in detail the size and form of the cells provided with cilia, as their variations in different situations have been and will be considered in connection with the physiological anatomy of different parts. In general structure, the ciliary processes are entirely homogeneous, and gradually taper from their attachment to the cell to an extremity of excessive tenuity. Although anatomists, from time to time, have described striæ at the bases of the cilia, and have attempted to explain their motion by a kind of muscular action, no well-defined structure has ever been actually demonstrated in their substance.

Certain currents were observed in the infusoria, mollusca, and other of the lower order of animals, long before the structure of the cilia had been accurately described; but in 1835, Purkinje and Valentin, in a very elaborate memoir, described these structures fully, and noted the situations

in which they are to be found in the human subject.[1] Their presence has been demonstrated on the following surfaces: The respiratory passages, including the nasal fossæ, the pituitary membrane, the summit of the larynx, the bronchial tubes, the superior surface of the velum palati, and the Eustachian tubes; the sinuses about the head; the lachrymal sac and the internal surface of the eyelids; the genital passages of the female, from the middle of the neck of the uterus to the extremities of the Fallopian tubes; and the ventricles of the brain. They probably exist also at the neck of the capsule of Müller, in the cortical substance of the kidney. In these situations, to each cell of conoidal epithelium are attached from six to twelve prolongations,[2] about $\frac{1}{25000}$ of an inch in thickness at their base, and from $\frac{1}{5000}$ to $\frac{1}{4000}$ of an inch in length.[3] The appearance of the cilia in detached cells is represented in Fig. 15. When seen *in situ*, they appear regularly disposed on the surface, are of nearly equal length, and are all slightly inclined in the direction of the opening of the cavity lined by the membrane.

FIG. 15.

Ciliated epithelium. (LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 579.)

The ciliary motion is one of the most beautiful physiological demonstrations that can be made with the microscope. By scraping the roof of the mouth of a living frog, the mucous membranes of the respiratory passages in a warm-blooded animal just killed, the beard of the oyster or clam, and placing the preparation, moistened with a little serum, under a magnifying power of about two hundred and

[1] PURKINJE AND VALENTIN, *Discovery of Continual Vibratory Motions, produced by Cilia, as a general Phenomenon in Reptiles, Birds, and Mammiferous Animals.—Edinburgh New Philosophical Journal*, 1835, vol. xix., p. 118, *et seq.*

[2] BÉCLARD, *Traité élémentaire de physiologie humaine*, Paris, 1859, p. 497.

[3] POUCHET, *Précis d'histologie humaine*, Paris, 1864, p. 189.

fifty diameters, the currents produced in the liquid will be strikingly exhibited. The movements may be studied in detached cells, in the human subject, by introducing a feather into the nose, when a few cells will be removed with the mucus, and can be observed in the same way.[1] This demonstration serves to show the similarity between the movements in man and in the lower orders of animals. When the movements are seen in a large number of cells *in situ*, the appearance is very graphically illustrated by the apt comparison of Henle to the undulations of a field of wheat agitated by the wind.[2] In watching this movement, it is usually seen to gradually diminish in rapidity, until what at first appeared simply as a current, produced by movements too rapid to be studied in detail, becomes revealed as distinct undulations, in which the action of individual cilia can be readily studied. Purkinje and Valentin describe several kinds of movement,[3] but the most common is a bending of the cilia, simultaneously or in regular succession, in one direction, followed by an undulating return to the perpendicular. The other movements, such as the infundibuliform, in which the point describes a circle around the base, the pendulum-movement, etc., are not common, and are unimportant.

The combined action of the cilia upon the surface of a mucous membrane, moving as they do in one direction, is to produce currents of considerable power. This may be illustrated under the microscope by covering the surface with a liquid holding little solid particles in suspension. In this case the granules are tossed from one portion of the field to another with considerable force. It is not difficult, indeed, to measure in this way the rapidity of the ciliary currents. In the frog it has been estimated at from $\frac{1}{250}$ to $\frac{1}{175}$ of an inch per second, the number of vibratile movements being from

[1] Béclard, *op. cit.*, p. 497.

[2] Henle, *Traité d'anatomie générale*, Paris, 1843, tome i., p. 263.

[3] *Loc. cit.*

seventy-five to one hundred and fifty per minute. In the fresh water polyp the movements are more rapid, being from two hundred and fifty to three hundred per minute.[1] There is no reliable estimate of the rapidity of the ciliary currents in man, but they are probably more active than in animals low in the scale.[2]

The movements of cilia, like those observed in fully-developed spermatozoids, seem to be entirely independent of nervous influence, and are affected only by purely local conditions. They will continue, under favorable circumstances, for more than twenty-four hours after death, and can be seen in cells entirely detached from the body when they are moistened with proper fluids. Béclard states that in the tortoise, the movement may be preserved for several weeks after the death of the animal.[3] When the cells are moistened with pure water, the activity of the movement is at first increased; but it soon disappears as the cells become swollen. Acids arrest the movement, but it may be excited by feeble alkaline solutions. All abnormal conditions have a tendency either to retard or to abridge the duration of the ciliary motion. It is true that when the movement is becoming feeble, it may be temporarily restored by very dilute alkaline solutions, but the ordinary stimuli, such as are capable of exciting muscular contraction, are without effect. Purkinje and Valentin, Sharpey, and others have attempted to excite the movements of cilia by galvanic stimulus, but without success.[4] Anæsthetics and narcotics, which have such a decided effect upon muscular action, have no influence upon the cilia.

It is useless to follow the speculations that have been

[1] BÉCLARD, *Traité élémentaire de physiologie*, Paris, 1859, p. 498.

[2] A pupil of M. Bernard, M. Calliburcès, has devised a very ingenious instrument for measuring the rapidity of the ciliary motion (BERNARD, *Leçons sur les propriétés des tissus vivants*, Paris, 1866, p. 139, *et seq.*).

[3] *Loc. cit.*

[4] SHARPEY, *Cyclopædia of Anatomy and Physiology*, London, 1835–'36, vol. i., p. 634, Article, *Cilia.*

advanced to account for the movement of cilia. There is no muscular structure, no connection with the nervous system, and there seems to be no possibility of explaining the movement except by a bare statement of the fact that the cilia have the property of moving in a certain way so long as they are under normal conditions. As regards the physiological uses of these movements, it is sufficient to refer to the physiology of the parts in which cilia are found, where the peculiarities of their action are considered more in detail. In the lungs and the air-passages generally, and the genital passages of the female, the currents are of considerable importance; but it is difficult to imagine the use of these movements in certain other situations, as the ventricles of the brain.

Movements due to Elasticity.—There are certain important movements in the body that are due simply to the action of elastic ligaments or membranes. These are entirely distinct from muscular movements, and are not even to be classed with the movements produced by the resiliency of muscular tissue, in which that curious property, called muscular tonicity, is more or less involved. Movements of this kind are never excited by nervous, galvanic, or other stimulus, but consist simply in the return of movable parts to a certain position after they have been displaced by muscular action, and the reaction of tubes after forcible distention, as in the walls of the large arteries.

Elastic Tissue.—Most writers of the present day adopt the division of the elastic tissue, first made by Henle,[1] into three varieties. This division relates to the size of the fibres; and all varieties are found to possess essentially the same chemical composition and general properties, including the elasticity for which they are so remarkable. On account of the yellow color of this tissue, presenting, as it does, a strong contrast to the white, glistening appearance

[1] Henle, *Traité d'anatomie générale*, Paris, 1848, tome i., p. 430.

of the inelastic fibres, it is frequently called the yellow elastic tissue.

The first variety of elastic tissue is composed of small fibres, generally intermingled with fibres of the ordinary inelastic tissue. These are sometimes called by the French, dartoic fibres. They possess all the chemical and physical characters of the larger fibres, but are excessively minute, measuring from $\frac{1}{25000}$ to $\frac{1}{6000}$ or $\frac{1}{5000}$ of an inch in diameter.[1] If we add acetic acid to a preparation of ordinary connective tissue, the inelastic fibres are rendered semitransparent, but the elastic fibres are unaffected and become very distinct. They are then seen isolated—that is, never arranged in bundles—always with a dark, double contour, branching, brittle, and when broken, their extremities curled and presenting a sharp fracture, like a piece of India-rubber. These fibres pursue a wavy course through the bundles of inelastic fibres in the areolar tissue and in most of the ordinary fibrous membranes, and here they exist as an accessory anatomical element. They are found in greater or less abundance in the situations just mentioned; also in the ligaments (but not the tendons); in the layers of involuntary muscular tissue; the true skin; the true vocal cords; the trachea, bronchial tubes, and largely in the parenchyma of the lungs; the external layer of the large arteries; and, in brief, in nearly all situations in which the ordinary connective tissue exists.

The second variety of elastic tissue is composed of fibres, larger than the first, ribbon-shaped, with well-defined outlines, anastomosing, undulating or curved in the form of the letter S, presenting the same curled ends and sharp fracture as the smaller fibres. These measure from $\frac{1}{5000}$ to $\frac{1}{3000}$ of an inch in diameter.[2] Their type is found in the ligamenta subflava and the ligamentum nuchæ. They are also found

[1] POUCHET, *Précis d'histologie humaine*, Paris, 1864, p. 62. In order to secure as much uniformity as possible in our measurements of microscopic structures, we have generally followed the French school of histologists.

[2] POUCHET, *loc. cit.*

in some of the ligaments of the larynx, the stylo-hyoid ligament, and the suspensory ligament of the penis. The form and arrangement of these fibres may be very beautifully demonstrated by tearing off a portion of the ligamentum nuchæ and lacerating it with needles in a drop of acetic acid. The action of the acetic acid renders the accessory structures of the ligament transparent, and the elastic fibres become very distinct. The same may be accomplished by boiling the tissue for a short time in caustic soda.

The third variety of elastic tissue can hardly be said to consist of fibres, their branches are so short and their anastomoses so frequent. This kind of structure is found forming the middle coat of the large arteries, and has already been described in connection with the vascular system.[1] The fibres are very large, flat, with numerous short branches, "which unite again with the trunk from which they originate or with adjacent fibres. In certain situations, the interstices are considerable, in proportion to the diameter of the fibres, and the anastomosing branches are given off at acute angles, so that they follow pretty closely the direction of the trunks, and the anastomoses do not disturb the longitudinal direction and parallelism of the fibres. Indeed, the anastomoses are so numerous, and the intervals so small, proportionally to the fibres, that we should believe we had under observation a reticulated membrane, presenting openings, rounded and oval, some large and others small."[2] These anastomosing fibres, forming the so-called fenestrated membranes, are arranged in layers, and the structure is sometimes called the lamellar elastic tissue.

The great resistance which the elastic tissue presents to chemical action serves to distinguish it from nearly every other structure in the body. We have already seen that it

[1] See vol. i., Circulation, p. 244.

[2] The above description, taken from Henle's general anatomy, conveys a very clear idea of the arrangement of the large elastic fibres in the "fenestrated membranes" (Henle, *Traité d'anatomie générale*, Paris, 1843, tome i., p. 4[illegible]).

is not affected by acetic acid or by boiling with caustic soda. It is not softened by heat, by prolonged boiling in water, but is slowly dissolved, without decomposition, by sulphuric, nitric, or hydrochloric acid, the solution not being precipitable by potash. Its organic base is a nitrogenized substance called elasticine;[1] containing carbon, hydrogen, oxygen, and nitrogen, without sulphur. This is supposed to be identical with the sarcolemma of the muscular tissue.[2]

The purely physical property of elasticity plays an important part in many of the animal functions. We have already had an example of this in the action of the large arteries in the circulation, and in the resiliency of the parenchyma of the lungs; and we shall have occasion, in treating of the functions of other parts, to refer again to the uses of elastic membranes and ligaments. The ligamenta subflava and the ligamentum nuchæ are important in aiding to maintain the erect position of the body and head, and to restore this position when flexion has been produced by muscular action. Still, the contraction of muscles is also necessary to keep the body in the vertical position.

Muscular Movements.

Muscular movements are observed only in the higher classes of animals. Low in the scale of animal life, we have the contractions of amorphous substance and ciliary motion; and in some vegetables, movements, even attended with locomotion, have been observed. These facts make the absolute distinction between the two kingdoms a question of some difficulty; but in animals only do we have separate muscular systems.

The muscular movements capable of being excited by stimulus of various kinds are divided into voluntary and involuntary; and generally there is a corresponding divi-

[1] See vol. i., Introduction, p. 91

[2] ROBIN ET VERDEIL, *Traité de chimie anatomique*, Paris, 1853, tome iii., p. 364.

sion of the muscles as regards their minute anatomy. The latter, however, is not absolute; for there are certain involuntary functions, like the action of the heart or the movements of deglutition, that require the rapid, vigorous contraction characteristic of the voluntary muscular tissue; and here we do not find the structure of the involuntary muscles. With a few exceptions, however, the anatomical division of the muscular tissue into voluntary and involuntary is sufficiently distinct.

Physiological Anatomy of the Involuntary Muscles.—We have so often described this tissue, as it is found in the vascular system, the digestive organs, skin, and other situations, that it will not be necessary, in this connection, to give more than a sketch of its structure and mode of action.

The involuntary muscular system presents a striking contrast to the voluntary muscles, not only in its minute anatomy and mode of action, but in the arrangement of its fibres. While the voluntary muscles are almost invariably attached by their two extremities to movable parts, the involuntary muscles form sheets or membranes in the walls of hollow organs, and by their contraction simply modify the capacity of the cavities which they enclose.

Various names have been given to this tissue to denote its distribution, mode of action, or structure. The name involuntary muscle indicates that its contraction is not under the control of the will; and this is the fact, these muscles being chiefly animated by the sympathetic system of nerves, while the voluntary muscles are supplied mainly from the cerebro-spinal system. On account of the peculiar structure of these fibres, they have been called muscular fibre-cells, smooth muscular fibres, pale fibres, non-striated fibres, fusiform fibres, and contractile cells. The distribution of these fibres to parts concerned in the organic or vegetative functions, as the alimentary canal, has given

them the name of organic muscular fibres, or fibres of organic, or vegetative life.

It is difficult to isolate the individual fibres of this tissue in microscopical preparations; and when seen *in situ*, their borders are faint, and we can make out their arrangement best by the appearance of their nuclei. Robin recommends soaking the tissue for a few days in a mixture of one part of ordinary nitric acid to ten of water.[1] This renders the fibres dark and granular, makes their borders very distinct, and frequently some of them become entirely isolated. The nuclei, however, are obscured. In their natural condition, the fibres are excessively pale, very finely granular, flattened, and of an elongated spindle-shape, with a very long, narrow, almost linear nucleus in the centre. The nucleus generally has no nucleolus, and it is sometimes curved, or shaped like the letter S. The ordinary length of these fibres is about $\frac{1}{500}$, and their breadth about $\frac{1}{4000}$ of an inch. In the gravid uterus they undergo remarkable hypertrophy, measuring here from $\frac{1}{80}$ to $\frac{1}{50}$ of an inch in length, and $\frac{1}{2000}$ of an inch in breadth.[2] The peculiarities of their structure in the uterus will be fully considered under the head of generation.

In the contractile sheets formed of the involuntary muscular tissue, the fibres are arranged side by side, closely adherent, and their extremities, as it were, dove-tailed into each other. Generally the borders of the fibres are regular and their extremities simple; but sometimes the ends are forked, and the borders present one or more little projections. It is very seldom that we see the fibres in a single layer, except in the very smallest arterioles. Usually the layers are multiple, being superimposed in regular order. The action of acetic acid is to render the fibres pale, so that their outlines become almost indistinguishable, and to bring

[1] ROBIN, *Recherches sur quelques particularités de la structure des capillaires de l'encéphale.—Journal de la physiologie*, Paris, 1859, tome ii., p. 541.

[2] POUCHET, *op. cit.*, p. 65.

out the nuclei more strongly. If we have an indistinct sheet of this tissue in the field of view, the addition of acetic acid, by bringing out the long, narrow, and curved nuclei arranged in regular order, and rendering the fibrous and other structures more transparent, will often enable us to recognize its character.

Contraction of the Involuntary Muscular Tissue.—The mode of contraction of the involuntary muscles is peculiar. It does not take place immediately upon the reception of a stimulus, applied either directly or through the nerves, but is gradual, enduring for a time and then followed by slow and gradual relaxation. A description of the peristaltic movements of the intestines gives a perfect idea of the mode of contraction of these fibres, with the gradual propagation of the stimulus along the alimentary canal, as the food makes its impression upon the mucous membrane.[1] An equally striking illustration is afforded by labor-pains. These are due to the muscular contractions of the uterus, and last from a few seconds to one or two minutes.[2] Their gradual access, continuation for a certain period, and gradual disappearance coincide exactly with the history of the contractions of the involuntary muscular fibres.

The strong points of contrast between the mode of action of the striated and the smooth muscular fibres are very well brought out in a recent paper by MM. Legros and Onimus. These observers, after carefully studying the structure and properties of the "muscles of vegetative life," give, in substance, the following *résumé* of their physiological action:

The contraction is slow, and the fibres return slowly to a condition of repose. The movements are always involuntary. Peristaltic action is the rule; and the contraction takes place progressively and without oscillations. Con-

[1] See vol. ii., Digestion, p. 376, *et seq.*

[2] CAZEAUX, *A Theoretical and Practical Treatise on Midwifery*, Philadelphia, 1857, p. 123.

tractility persists for a long time after death. Arrest of function is followed by little or no atrophy, and hypertrophy is very marked as the result of exaggerated action. Excitation of the nerves has less influence upon contraction of these fibres than direct excitation of the muscles. The involuntary muscular tissue is regenerated very rapidly, while the structure of the voluntary muscles is restored with great difficulty after destruction or division.[1]

Physiological Anatomy of the Voluntary Muscles.—A voluntary muscle is the most highly organized, and is possessed of the most varied endowments, of all living structures. It contains, in addition to its own peculiar contractile substance, fibres of inelastic and elastic tissue, adipose tissue, numerous blood-vessels, nerves, and lymphatics, with certain nuclear and cellular anatomical elements. The muscular system constitutes by far the greatest part of the organism, and its nutrition consumes a large proportion of the reparative material of the blood, while its disassimilation furnishes a corresponding quantity of excrementitious matter. The condition of the muscular system, indeed, is an almost unfailing evidence of the general state of the body, allowing, of course, for peculiarities in different individuals. Among the characteristic properties of the muscles are, elasticity, a constant and insensible tendency to contraction, called tonicity, the power of contracting forcibly on the reception of a proper stimulus, called irritability, a peculiar kind of sensibility, and the faculty of generating galvanic currents. The relations of particular muscles, as taught by descriptive anatomy, involve special functions; but the most interesting physiological points connected with this system relate to the general properties and functions of the muscles, and must necessarily be prefaced with a sketch of their general anatomy.

[1] LEGROS ET ONIMUS, *De la contraction des muscles de la vie végétative.—Journal de l'anatomie*, Paris, 1869, tome vi., p. 435.

It has been demonstrated by minute dissection that all of the red, or voluntary muscles are made up of a great number of microscopic fibres, known as the primitive muscular fasciculi. These are called red, striated, or voluntary fibres, or the fibres of animal life. Their structure is complex, and they may be subdivided longitudinally into fibrillæ, and transversely into disks, so that it is somewhat doubtful as to what is, strictly speaking, the ultimate anatomical element of the muscular tissue.

A primitive muscular fasciculus runs the entire length of the muscle, and is enclosed in its own sheath, without branching or inosculation. This sheath contains the true muscular substance only, and is not penetrated by blood-vessels, nerves, or lymphatics. If we view with the microscope a thin transverse section of a muscle, the divided ends of the fibres will present an irregularly-polygonal form with rounded corners. They seem to be cylindrical, however, when viewed in their length and isolated. Their color by transmitted light is a delicate amber, resembling somewhat the color of the blood-corpuscles.

The primitive fasciculi vary very much in size in different individuals, and in the same individual under different conditions and in different muscles. As a rule they are smaller in young persons and in females than in adult males. They are comparatively small in persons of slight muscular development. In persons of great muscular vigor, or when the general muscular system or particular muscles have been increased in size and power by exercise, the fasciculi are relatively larger. It is probable that the physiological increase in the size of a muscle from exercise is due to an increase in the size of the preëxisting fasciculi, and not to the formation of any new elements. In young persons the fasciculi are from $\frac{1}{1700}$ to $\frac{1}{1200}$ of an inch in diameter. In the adult they measure from $\frac{1}{450}$ to $\frac{1}{250}$ of an inch.[1]

The appearance of the primitive muscular fasciculi

[1] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Musculaire*.

under the microscope is characteristic and unmistakable. They present regular transverse striæ, formed of alternating dark and clear bands about $\frac{1}{25000}$ of an inch wide. These are generally very distinct in healthy muscles. In addition we frequently observe longitudinal striæ, not so distinct, and quite difficult to follow to any extent in the length of the fasciculus, but tolerably well marked, particularly in muscles that are habitually exercised. The muscular substance, presenting this peculiar striated appearance, is enclosed in an excessively thin but elastic and resisting tubular membrane, called the sarcolemma, or myolemma. According to Robin,[1] the sarcolemma is composed of the same substance as the elastic tissue. This envelope cannot be seen in ordinary preparations of the muscular tissue; but it frequently happens that the contractile muscular substance is broken, leaving the sarcolemma intact, which gives a good view of the membrane and conveys an idea of its strength and elasticity. Attached to the inner surface of the sarcolemma, are numerous small, elongated nuclei with their long diameter in the direction of the fasciculi. These are not usually well seen in the unaltered muscle, but the addition of acetic acid renders the muscular substance pale and destroys the striæ, when the nuclei become very distinct.

Water, after a time, acts upon the muscular tissue, rendering the fasciculi somewhat paler and larger. Acetic acid and alkaline solutions efface the striæ, and the fibres become semitransparent.

In fasciculi that are slightly decomposed, there is frequently a separation at the extremity into numerous smaller fibres, called fibrillæ. These, when isolated, present the same striated appearance as the primitive fasciculus; viz., alternate dark and light portions. They measure about $\frac{1}{25000}$ of an inch in diameter, and their number, in the largest primitive fibres, is estimated by Kölliker at about two thou-

[1] *Loc. cit.*

sand.[1] The structure of the fibrillæ, which are regarded by many as the anatomical elements of the muscular tissue, has been very closely studied by Rouget; and, although all of his observations, particularly those with regard to the spiral form of the fibrillæ, have not been confirmed, there can be hardly any doubt that their structure is uniform, the appearance of alternate dark and light segments being due to differences in thickness.[2] In fact, it is well known that water, by its simple mechanical action, swells the fibrillæ, and causes the striæ to disappear.

Late researches have shown that the interior of each primitive fasciculus is penetrated by an excessively delicate membrane, closely surrounding the fibrillæ. This arrangement may be distinctly seen in a thin section of a fibre treated with a solution of salt in water in the proportion of five parts per thousand.[3] The arrangement of this membrane, which is nothing more nor less than a series of tubular sheaths for the fibrillæ, is a strong argument in favor of the view that the fibrilla is the anatomical element of the muscular tissue.

By the action of certain reagents, such as alcohol, hydrochloric acid, or gastric juice, the primitive fasciculi may be separated into disks corresponding to the transverse striæ. Bowman, in his elaborate investigations into the structure of the muscles, noted this fact, and concluded that the cleavage in this direction was as easily effected as the separation into fibrillæ. He regarded the primitive fasciculi as composed of fibrillæ, and these as made up of little particles, alternately dark and light, which he called sarcous elements.[4] Subsequent investigations, however, have not en-

[1] Kölliker, *Éléments d'histologie humaine*, Paris, 1868, p. 207.

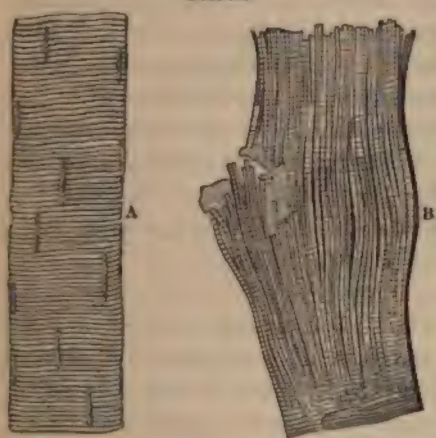
[2] Rouget, *Sur les phénomènes de polarization qui s'observent dans quelques tissus.—Journal de la physiologie*, Paris, 1862, tome v., p. 263, *et seq.*, and *Mémoire sur les tissus contractiles et la contractilité.*—Id., 1863, tome vi., p. 647, *et seq.*

[3] Kölliker, *Éléments d'histologie humaine*, Paris, 1868, p. 201.

[4] Bowman, *On the Minute Structure and Movements of Voluntary Muscle*—*Philosophical Transactions*, London, 1840, p. 457, *et seq.*

tirely confirmed this view; and the separation into disks is now pretty generally regarded as artificial.

Fig. 16.



Voluntary muscular fibres. A, Transverse striæ and nuclei of a primitive fasciculus (magnified 250 diameters); B, longitudinal striæ and fibrillæ of a primitive fasciculus in which the sarcolemma has been lacerated at one point by pressure. (SAPPEY, *Traité d'anatomie*, Paris, 1868, tome ii., p. 22.)

When we come to the question of the real anatomical element of the muscular tissue, there are only two reasonable views that present themselves. One is that all subdivision of the primitive fasciculus is artificial, and that it, with its investing membrane, the sarcolemma, is the true element. An argument in favor of this opinion is that the tissue is most readily separated into fasciculi, each enclosed in its own membrane, and not penetrated by vessels, nerves, or lymphatics; while the fibrillæ are situated in a reticulum of canals, from which they cannot readily be isolated. The other opinion, that the fibrillæ are the ultimate elements, is based on the fact that these little fibres present the striæ and all the anatomical characteristics of the primitive fasciculi, and that by far the most natural and easy mode of separation of these fasciculi is in a longitudinal direction. The question of adopting one or the other of these views is not of very great physiological importance.

Fibrous and Adipose Tissue in the Voluntary Muscles.—The structure of the muscles strikingly illustrates the relations between the principal and the accessory anatomical elements of tissues. The characteristic or principal element

is, of course, the muscular fibre or fibrilla; but we also find in the substance of the muscles certain anatomical elements, not peculiar to the muscles, and merely accessory in their function, but none the less necessary to their proper constitution. For example, every muscle is composed of a number of primitive fasciculi; but these are gathered into secondary bundles, which in turn are collected into bundles of greater and greater size, until, finally, the whole muscle is enveloped in its sheath, and is penetrated by a fibrous connective substance. We find, probably, in the muscles, the best illustration of the structure of what is known as the connective tissue.

Connective Tissue.—We have already had occasion to refer to certain of the elements of connective tissue, more especially the inelastic and elastic fibres. In this connection we shall treat specially of the connective tissue of the muscles; but our description will answer for almost all situations in which fibrous tissue exists merely for the purpose of holding parts together. In the muscles we have a membrane holding a number of the primitive fasciculi into secondary bundles. This is known as the perimysium. The fibrous membranes that connect together these secondary bundles with their contents are enclosed in a sheath enveloping the whole muscle, sometimes called the external perimysium. The peculiarity of these membranes, and their distinction from the sarcolemma, is that they have a fibrous structure and are connected together throughout the muscle, while the tubes forming the sarcolemma are structureless, and each one is distinct.

The name now most generally adopted for the tissue under consideration is connective tissue. It has been called cellular, areolar, or fibrous, but most of these names were given to it without a clear idea of its structure. Its principal anatomical element is a fibre of excessive, almost immeasurable, tenuity, wavy, and with a single contour. These

fibres are collected into bundles of very variable size, and are held together by an adhesive amorphous substance. The wavy lines that mark the bundles of fibres give them a very characteristic appearance.

The direction and arrangement of the fibres in the various tissues present marked differences. In the loose areolar tissue beneath the skin and between the muscles, and in the loose structure surrounding some of the glands and connecting the sheaths of blood-vessels and nerves to the adjacent parts, the bundles of fibres form a large net-work, and are very wavy in their course. In the strong, dense membranes, as the aponeuroses, the proper coats of many glands, the periosteum and perichondrium, and the serous membranes, the waves of the fibres are shorter, and the fibres themselves interlace much more closely. In the ligaments and tendons, the fibres are more nearly straight, and are all arranged longitudinally.

On the addition of acetic acid, the bundles of inelastic fibres swell up, become semitransparent, and the nuclei and elastic fibres are brought out. The proportion of elastic fibres differs very much in different situations, but they are all of the smallest variety, and present a striking contrast to the inelastic fibres in their form and size. Though they are still very small, they always present a double contour.

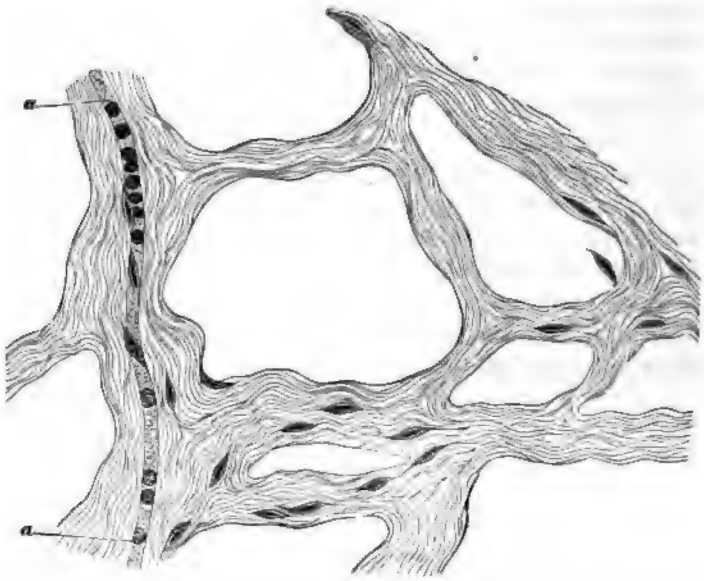
Certain cellular and nuclear elements are always found in the connective tissue. The cells have been described under the name of connective-tissue cells. They are very irregular in size and form, some of them being spindle-shaped or caudate, and others star-shaped. They possess one, and sometimes two or three clear, ovoid nuclei, with distinct nucleoli. On the addition of acetic acid the cells disappear, but the nuclei are unaffected. These are the fibro-plastic elements of Lebert,[1] and the embryo-plastic elements of Robin.[2]

[1] LEBERT, *Physiologie pathologique*, Paris, 1845, tome ii., page 120.

[2] LITTRÉ ET ROBIN, *Dictionnaire de médecine*, Paris, 1865, Article, *Embryoplastique*.

It is impossible to give any accurate measurements of the cells, on account of their great variations in size. The length of the nuclei is from $\frac{1}{3000}$ to $\frac{1}{2500}$ of an inch, and their diameter, from $\frac{1}{5000}$ to $\frac{1}{4000}$ of an inch.[1] The appearance of the connective tissue, with a few cells and nuclei, is represented in Fig. 17.

FIG. 17.



Loose net-work of connective tissue from the human subject, showing the fibres and cells. *a, a*, a capillary blood-vessel. (ROLLETT, in STRICKER, *Handbuch der Lehre von den Geweben*, Leipzig, 1868, S. 57.)

Between the muscles, and in the substance of the muscles between the bundles of fibres, there always exists a greater or less quantity of adipose tissue in the meshes of the fibrous structure.

Blood-vessels and Lymphatics.—The muscles are abundantly supplied with blood-vessels, generally by a number of small arteries, with two satellite veins. The capillary ar-

[1] ROBIN, *loc. cit.*

rangement in this tissue is peculiar. From the smallest arterioles, capillary vessels are given off, arranged in a network with tolerably-regular, oblong, rectangular meshes, their long diameter following the direction of the fibres. These envelop each primitive fasciculus, enclosing it completely, the artery and vein being on the same side. The capillaries are the smallest in the whole vascular system. When distended with blood they are from $\frac{1}{4500}$ to $\frac{1}{3750}$ of an inch in diameter; and when empty their diameter is from $\frac{1}{7000}$ to $\frac{1}{5500}$ of an inch.[1]

The arrangement of the lymphatics in the muscles has never been definitely ascertained. There are numerous lymphatics surrounding the large vascular trunks of the extremities and of the abdominal and thoracic walls, which, it would appear, must come from the substance of the muscles; but they have never been traced to their origin. Sappey has succeeded in injecting lymphatics upon the surface of some of the larger muscles, but never has been able to follow them into the muscular substance.[2]

Connection of the Muscles with the Tendons.—It is now generally admitted that the primitive muscular fasciculi terminate in little conical extremities, which are received into corresponding depressions in the bundles of fibres composing the tendons; but this union is so close, that the muscle or the tendon may be ruptured without a separation at the point of juncture. In the penniform muscles this arrangement is quite uniform and elegant. In other muscles it is essentially the same, but the perimysium seems to be continuous with the loose areolar tissue enveloping the corresponding tendinous bundles.

Chemical Composition of the Muscles.—We are as yet so little acquainted with the exact constitution of the nitrogenized constituents of the body, that we cannot appreciate the

[1] Kölliker, *Eléments d'histologie humaine*, Paris, 1868, p. 220.

[2] Sappey, *Traité d'anatomie descriptive*, Paris, 1868, tome ii., p. 27.

nature of all the proximate principles that exist in the muscular substance. The most important of these is musculine. This resembles the fibrin of the blood, but presents certain points of difference in its behavior to reagents, by which it may be readily distinguished. One of its peculiar properties is that it is dissolved at an ordinary temperature by a mixture of one part of hydrochloric acid and ten of water.

The muscular substance is permeated by a fluid, called the muscular juice, which contains a peculiar coagulable principle called myosine.

Combined with the organic principles, we find a great variety of mineral salts in the muscular substance, that cannot be separated without incineration. Certain excrementitious matters have also been found in the muscles; and probably nearly all of those eliminated by the kidneys exist here, though they are taken up by the blood as fast as they are produced, and are consequently detected with difficulty. The muscles also contain inosite, inosic acid, lactic acid, and certain other acids of fatty origin. During life the muscular fluid is slightly alkaline, but it becomes acid soon after death. The muscle itself, during contraction, has an acid reaction.[1] According to Gavarret, the muscular juice is alkaline or neutral after moderate exercise, as well as during complete repose; but he states that when a muscle is made to undergo excessive exercise, the lactic acid exists in greater quantity, and the reaction becomes acid.[2]

Physiological Properties of the Muscles.

The general properties of the striated muscles, as distinguished from all other tissues except the involuntary muscles, are as follows: 1. elasticity; 2. tonicity; 3. sensibility of a peculiar kind; 4. contractility, or irritability. These are all necessary to the physiological action of the muscles. Their

[1] Budge, *Lehrbuch der speciellen Physiologie des Menschen*, Leipzig, 1862, S. 534.

[2] Gavarret, *Les phénomènes physiques de la vie*, Paris, 1869, p. 125.

elasticity is brought into play in opposing muscles or sets of muscles; one set acting to move a part and extend the antagonistic muscles, which, by virtue of their elasticity, retract when the extending force is removed. Their tonicity is an insensible, and more or less constant contraction, by which the action of opposing muscles is balanced when both are in the condition of what we call repose. Their sensibility is peculiar, and is expressed chiefly in the sense of fatigue, and in the appreciation of weight and resistance to contraction. Their contractility, or irritability is the property which enables them to contract and exert a certain amount of mechanical force under the proper stimulus. All of these general properties strictly belong to physiology, as do some special acts that are not necessarily involved in the study of ordinary descriptive anatomy.

Elasticity of Muscles.—The true muscular substance contained in the sarcolemma is eminently contractile; and though it may possess a certain degree of elasticity, this property is most strongly marked in the accessory anatomical elements. The interstitial fibrous tissue is loose and possesses a certain number of elastic fibres, and, as we have seen, the sarcolemma is very elastic. It is probably the sarcolemma that gives to the muscles their retractile power after simple extension.

It is unnecessary to follow out in detail all of the numerous experiments that have been made upon the elasticity of muscles. There is a certain limit, of course, to their perfect elasticity (understanding by this the degree of extension that is followed by complete retraction), and this cannot be exceeded in the human subject without dislocation of parts. In some late experiments by Marey, it was found that the gastrocnemius muscle of a frog, detached from the body, could be extended about one-fiftieth of an inch by a weight of a little more than three hundred grains. This weight, however, did not extend the muscle beyond the

limit of perfect elasticity. The muscle of a frog of ordinary size was extended beyond the possibility of complete restoration by a weight of about seven hundred and fifty grains.[1] Marey also showed that fatigue of the muscles increased their extensibility and diminished their power of subsequent retraction. This fact has its application to the physiological action of muscles; for it is well known that they are unusually relaxed during fatigue after excessive exertion; and, as we should expect, they are at that time more than ordinarily extensible.

Muscular Tonicity.—The healthy muscles have an insensible and constant tendency to contract, which is more or less dependent upon the action of the motor nerves. If, for example, a muscle be cut across in a surgical operation, the divided extremities become permanently retracted; or if the muscles be paralyzed on one side of the face, the muscles upon the opposite side insensibly distort the features. It is difficult to explain these phenomena by assuming that tonicity is due to reflex action, for there is no evidence that the contraction takes place as the consequence of a stimulus. All that we can say is, that a muscle, not excessively fatigued, and with its nervous connections intact, is constantly in a state of insensible contraction, more or less marked, and that this is an inherent property of all of the contractile tissues.

Sensibility of the Muscles.—The muscles possess to an eminent degree that kind of sensibility which enables us to appreciate the power of resistance, immobility, and elasticity of substances that are grasped, on which we tread, or which, by their weight, are opposed to the exertion of muscular power. It is by the appreciation of weight and resistance that we regulate the amount of force required to accomplish any muscular act. These properties refer chiefly to simple

[1] MAREY, *Du mouvement dans les fonctions de la vie*, Paris, 1868, pp. 289, 301.

muscular efforts. After long-continued exertion, we appreciate a sense of fatigue that is peculiar to the muscles. It is difficult to separate this entirely from the sense of nervous exhaustion, but it seems to be, to a certain extent, distinct; for when suffering from the fatigue that follows over-exertion, it seems as though we could send a nervous stimulus to the muscles, to which they are, for the time, unable to respond. When we come to consider fully the subjects of muscular and nervous irritability, we shall see that these two properties are entirely distinct, and that we may exhaust or destroy the one without influencing the other.

When the muscles are thrown into spasm or tetanic contraction, a peculiar sensation is produced, entirely different from painful impressions made upon the ordinary sensitive nerves. In the cramps of cholera, tetanus, or the convulsions from strychnine, these distressing sensations are very marked. The so-called recurrent sensibility of the anterior roots of the spinal nerves is probably due to the tetanic contractions produced by galvanizing these filaments. This question, however, will be taken up again in connection with the nervous system.

If the muscles possess any general sensibility, it is very faint. A muscle may be lacerated or irritated in any way without producing actual pain, though we always can appreciate the contraction produced by irritants, and the sense of tension when the muscles are drawn upon.

Muscular Contractility, or Irritability.—Physiologists now regard muscular irritability as synonymous with contractility; and perhaps the latter term more nearly expresses the fact, though the term irritability, applied to the nerves, and even of late years to the glands, is one very generally used.

By irritability we understand a property belonging to highly-organized parts, which enables them to perform certain peculiar and characteristic functions in obedience to a proper stimulus. In the sense in which the term is gen-

erally received, it is proper to apply it to any tissue or organ that performs its vital function, so-called, under a natural or artificial stimulus. The nerves receive impressions and carry a stimulus to the muscles, causing them to contract. This property, which is always present during life under normal conditions, and persists for a certain period after death, is called nervous irritability. It has lately been shown that the application of a proper stimulus will induce secretion by the glands; and Bernard has called this glandular irritability.[1] The application of a stimulus to the muscular tissue causes the fibres to contract; and this is muscular irritability. As it always involves contraction, and is extinct only when the muscles can no longer act, it is equally proper to call this property contractility. No property, such as we understand by this definition of irritability, is manifested by tissues or organs that have purely passive or mechanical functions, such as bones, cartilages, and fibrous or elastic membranes. Irritability can only be applied properly to nerves or nerve-centres, contractile structures, and glands.

During life and under normal conditions, the muscles will always contract in obedience to a proper stimulus applied either directly or through the nerves. In the natural action of the organism, this contraction is always induced by nervous influence through reflex action or volition. Still, a muscle may be living and yet have lost its contractility. For example, after a muscle has been for a long time paralyzed and disused, the application of the most powerful galvanic excitation will fail to induce contraction. But when we examine such a muscle with the microscope, it is found that the nutrition has become profoundly affected, and that the contractile substance has disappeared, giving place to inert fatty matter. Muscular contractility persists for a certain time after death and in muscles separated from the body; and this fact has been taken advantage of by physiologists in the study of the so-called vital properties of the

[1] See page 24.

muscular tissue. We have already seen that a muscle detached from the living body continues for a time to respire, and probably undergoes some of the changes of disassimilation observed in the organism. So long as these changes are restricted to the limits of physical and chemical integrity of the fibre, contractility remains. As these processes are very slow in the cold-blooded animals, the irritability of all the parts persists for a considerable time after death. We have repeatedly demonstrated muscular contractility, several days after death, in alligators and turtles.

In the human subject and the warm-blooded animals, the muscles cease to respond to excitation a few hours after death, though the time of disappearance of irritability is very variable. Nysten, in a number of experiments upon the disappearance of contractility in the human subject after decapitation, found that different parts lost their contractility at different periods, but that generally this depended upon exposure to the air. With the exception of the right auricle of the heart, the muscles of the voluntary system were the last to lose their irritability. In one instance, certain of the voluntary muscles that had not been exposed retained their contractility seven hours and fifty minutes after death.[1] The observations of Longet and Masson show that a galvanic shock, sufficiently powerful to produce death, instantly destroys the irritability of the muscular tissue and of the motor nerves.[2]

One of the most important questions to determine with regard to muscular irritability is whether it be a property inherent in the muscular tissue or derived from the nervous system. The fact that muscles can be excited to more powerful and regular contractions by stimulating the motor nerves than by operating directly upon their substance and the great difficulty in tracing the nerves to their termination

[1] NYSTEN, *De la contractilité des organes musculaires.—Recherches de physiologie et de chimie pathologiques*, Paris, 1811, p. 306, *et seq.*

[2] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 602.

in the muscles have led to the view that muscular contractility is dependent upon nervous influence, and consequently that the muscles have no irritability or contractility, as a property inherent in their own substance. This doctrine, however, cannot be sustained. Bowman, in the course of his researches into the structure and movements of voluntary muscles, speaks of seeing the individual fibres contract after they had been isolated and removed from all connection with the nervous system; and this has been frequently observed.[1]

The experiments of Longet, published in 1841, presented almost conclusive proof of the independence of muscular irritability. He resected the facial nerve, and found that it ceased to respond to mechanical and galvanic stimulus, or, in other words, lost its irritability, after the fourth day. Operating, however, upon the muscles supplied exclusively with filaments from this nerve, he found that they responded promptly to mechanical and galvanic irritation, and continued to contract, under stimulation, for more than twelve weeks.[2] In some farther experiments it was shown that while the contractility of the muscles could be seriously influenced through the nervous system, this was effected only by modifications in their nutrition. When the mixed nerves were divided, the nutrition of the muscles was generally disturbed; and although muscular irritability persisted for some time after the nervous irritability had disappeared, it became very much diminished at the end of six weeks.

These experiments are very striking and satisfactory; but the whole question was definitively settled by the observations of Bernard on the peculiar influence of the woorara poison and the sulphocyanide of potassium. As the result of these experiments, it was ascertained that some varieties of woorara destroy the irritability of the motor nerves, leaving the sensitive filaments intact. If a frog be poisoned by introducing

[1] Bowman, *The Minute Structure and Movements of Voluntary Muscle.—Philosophical Transactions*, London, 1840, p. 488, *et seq.*

[2] Longet, *Traité de physiologie*, Paris, 1869, tome ii., p. 606.

a little of this agent under the skin, irritation, galvanic or mechanical, applied to an exposed nerve, fails to produce the slightest muscular contraction; but if the stimulus be applied directly to the muscles, they will contract vigorously. In this way the nerves are, as it were, dissected out from the muscles; and the discovery of an agent that will paralyze the nerves, without affecting the muscles, is conclusive proof that the irritability of these two systems is entirely distinct. A curious effect of the woorara, that we may note in passing, is that in an animal under its influence, the muscular irritability is intensified, and persists much longer after death than in animals not poisoned.[1] If a frog be poisoned with sulpho-cyanide of potassium, precisely the contrary effect will be observed; that is, the muscles will become insensible to excitation, while the nervous system is unaffected. This fact may be demonstrated by applying a tight ligature around the body in the lumbar region, involving all the parts except the lumbar nerves. If the poison be now introduced beneath the skin of the parts above the ligature, the anterior parts only are affected, because the vascular communication with the posterior extremities is cut off. If the exposed nerves be now galvanized, the muscles of the legs are thrown into contraction, showing that the nervous irritability remains. Reflex movements in the posterior extremities may also be produced by irritation of the parts above the ligature.[2]

These experiments, most of which we have frequently repeated, taken in connection with the observations of Longet, and the fact that isolated muscular fibres have been seen to contract, leave no doubt of the existence of an inherent and independent irritability in the muscular tissue. Contractions of muscles, it is true, are normally excited through the nervous system, and artificial stimulation of a motor or mixed nerve is the most efficient method of producing the simul-

[1] BERNARD, *Leçons sur les effets des substances toxiques et médicamenteuses*, Paris, 1857, pp. 277, 320, 353.

[2] BERNARD, *loc. cit.*, p. 354, *et seq.*

taneous action of all the fibres of a muscle, or set of muscles; but galvanic, mechanical, or chemical irritation of the muscles themselves will produce contraction, after the nervous irritability has been abolished.

The conditions under which muscular irritability exists are simply those of normal nutrition of the muscular tissue. When the muscles have become profoundly affected in their nutrition, as the result of section of the mixed nerves, or after prolonged paralysis, the irritability disappears and cannot be restored. The determination of the presence or absence of muscular contractility, in cases of paralysis, is one of the methods of ascertaining whether treatment directed to the restoration of the nervous power will be likely to be followed by favorable results. If the muscular irritability have entirely disappeared, it is almost useless to attempt to restore the functions of the part.

A great many experiments have been made upon the influence of the circulation on muscular irritability, chiefly with reference to the effects of tying large vessels. Among the most recent are those of Longet. He tied the abdominal aorta in five dogs, and found that voluntary motion ceased in about a quarter of an hour, and that the muscular irritability was extinct in two hours and a quarter. When the blood was restored, after three or four hours, by removing the ligature, the irritability and finally voluntary movement returned.[1] These experiments show that the circulation of the blood is necessary to the contractility of the muscles. Tying the vena cava did not affect the irritability of the muscles. In dogs in which this experiment was performed, the lower extremities preserved their contractility, and the voluntary movements were unaffected up to the time of death, which took place in twenty-six hours.[2]

The relations of muscular irritability to the circulation have been farther illustrated, in some very curious and in-

[1] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 616.
[2] LONGET, *op. cit.*, p. 618.

teresting experiments, by Dr. Brown-Séquard. The first observations were made upon two men executed by decapitation. Thirteen hours and ten minutes after death, when the muscular irritability had entirely disappeared and was succeeded by cadaveric rigidity, a quantity of fresh, defibrinated, venous blood, from the human subject, was injected into the arteries of one hand, and returned by the veins. It was afterward reinjected several times during a period of thirty-five minutes. The whole time occupied in the different injections was from ten to fifteen minutes. Ten minutes after the last injection, and about fourteen hours after death, the irritability was found to have returned, in a marked degree, in twelve muscles of the hand. There were only two muscles out of the nineteen in which the irritability could not be demonstrated. Three hours after, the irritability still existed, but it disappeared a quarter of an hour later. The second observation was essentially the same, except that defibrinated blood from the dog was used, and the experiments were made upon the muscles of the arm. The irritability was restored in all of the muscles, and was present, the cadaveric rigidity having disappeared, twenty hours after decapitation.[1]

These experiments are exceedingly interesting, as showing the dependence of irritability upon certain of the processes of nutrition, which are probably restored, though temporarily and imperfectly, by the injection of fresh blood. They are also important in connection with the cadaveric rigidity of muscles, a condition which follows the loss of their so-called vital properties. The subject of cadaveric rigidity will be fully discussed as one of the phenomena of death.

[1] BROWN-SÉQUARD, *Propriétés physiologiques et les usages du sang rouge et du sang noir.—Journal de la physiologie*, Paris, 1858, tome i., p. 108, *et seq.*

CHAPTER XVI.

MUSCULAR CONTRACTION.—PASSIVE ORGANS OF LOCOMOTION.

Changes in the form of the muscular fibres during contraction—*Secousse*, *Zückung*, or spasm—Spasm produced by artificial excitation—Mechanism of prolonged muscular contraction—Tetanus—Electric phenomena in the muscles—Muscular effort—Passive organs of locomotion—Physiological anatomy of the bones—Fundamental substance—Haversian rods—Haversian canals—Lacunæ—Canaliculi—Bone-cells, or corpuscles—Marrow of the bones—Medullocells—Myeloplaxes—Periosteum—Physiological anatomy of cartilage—Cartilage-cavities—Cartilage-cells—Fibro-cartilage.

The stimulus of the will, conveyed through the conductors of motor influences from the brain to a muscle or set of muscles, produces an impression upon the muscular fibres and causes them to contract. In parts where the muscles have been exercised and educated, this action is regulated with exquisite nicety, so that the most delicate, rapid, as well as powerful contractions may be produced. Certain movements, not under the control of the will, are produced as the result of unconscious reflection from a nervous centre, along the motor conductors, of an impression made upon sensitive nerves. During this action, certain important phenomena are observed in the muscles themselves. They change in form, consistence, and, to a certain extent, in their constitution; the different periods of their stimulation, contraction, and relaxation are positive and well-marked; their nutrition is for the time modified; they develop galvanic currents; and, in short, present a number of general phenomena, distinct from the results of their action, that are more or less interesting and important to the physiologist.

The most striking of the phenomena accompanying muscular action is shortening and hardening of the fibres. It is only necessary to observe the action of any well-developed muscle to appreciate these changes. The active shortening is shown by the approximation of the points of attachment, and the hardening is sufficiently palpable. The latter phenomenon is marked in proportion to the development of the true muscular tissue and its freedom from inert matter, such as fat. We have already seen that it is the muscular substance alone that has the property of contraction; and we have shown that this action increases the consumption of oxygen and probably of other matters, the production of carbonic acid and some other excrementitious principles, and develops heat.

Notwithstanding the marked and constant changes in the form and consistence of the muscles during contraction, the actual volume is unchanged, or it undergoes modifications so slight that they may practically be disregarded. Experiments on this point have been so uniform in their results, that it is hardly necessary to refer to them in detail. All modern observers accept the results of the older experiments in which muscles have been made to contract in a vessel of water connected with a small upright tube, showing that when the muscles are in active contraction as the result of a galvanic stimulus, the elevation of the liquid in the tube is unchanged. These old experiments have been recently repeated by Marey[1] and others, with more delicate and sensitive apparatus, and have been followed by the same results. It is evident, therefore, that a muscle, while it hardens and changes in form during contraction, does not sensibly change in its actual volume.

[1] MAREY, *Du mouvement dans les fonctions de la vie*, Paris, 1868, p. 269. The earlier experiments of this kind were made by Glisson, Blaine, Carlisle, Barzellotti, Prévost and Dumas, and some others. Prévost and Dumas used several large pieces of muscle, and their results were very satisfactory. (*Mémoire sur les phénomènes qui accompagnent la contraction de la fibre musculaire.—Journal de physiologie*, Paris, 1823, tome iii., p. 310.)

lar action, presents certain interesting peculiarities. We shall give, however, only the general characters of this action, without discussing in detail the complicated apparatus employed.[1]

According to Helmholtz, the whole period of a single contraction and relaxation of the gastrocnemius muscle of a frog is a little less than one-third of a second. The muscles of mammals and birds contract more rapidly, but with this exception, the essential characters of the contraction are the same. The following are the periods occupied by these different phenomena:[2]

Interval between stimulation and contraction	0″·020
Contraction	0″·180
Relaxation	0″·105
	0″·305

The duration of the electric current applied to the nerve is only 0″·0008. Contraction, however, does not follow immediately, there being an interval, called *pose*, of about one fiftieth of a second. The contraction then follows, succeeded by gradual relaxation, the former being a little longer than the latter.

This description represents the contraction of an entire muscle, but does not indicate the changes in form of the individual fibres, a point much more difficult to determine satisfactorily. It is pretty well established, however, that a single fibre, with its irritability unimpaired, becomes contracted and swollen at the point where the stimulation is applied. Now, the question is whether, in normal contraction of the fibres in obedience to the natural nervous stimulus, there be a uniform shortening of the whole fibre, a shortening of those portions only that are the seat of the

[1] A very good *résumé* of the general characters of a single muscular contraction (*secousse musculaire*) is given by Bernard, in his recent work on the properties of living tissues. (*Leçons sur les propriétés des tissus vivants*, Paris, 1866, p. 193, *et seq.*)

[2] BERNARD, *op. cit.*, p. 196.

terminations of the motor nerves, or a peristaltic shortening and swelling, rapidly running the length of the fibre.

The recent experiments of Aeby, which have been repeated and extended by Marey, demonstrate beyond a doubt that when one extremity of a muscle is excited, a contraction occurs at that point, and is propagated along the muscle in the form of a wave, exactly like the peristaltic action of the intestines, except that it is more rapid. Both Aeby and Marey have succeeded in measuring the rapidity of this wave, and find it to be about forty inches per second.[1] Applying this principle to the physiological action of muscles, Aeby advances the theory that shortening of the fibres takes place wherever a stimulus is received, and that this is propagated in the form of a wave, which meets in its course another wave starting from a different point of stimulation. As we know

FIG. 18.

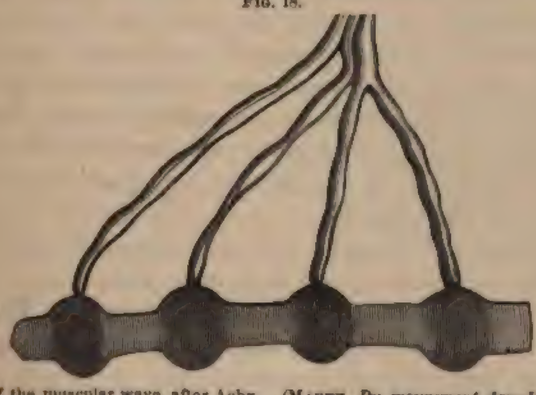


Diagram of the muscular wave, after Aeby. (MAREY, *Du mouvement dans les fonctions de la vie*, Paris, 1868, p. 282.)

that the motor nerves terminate at different points by becoming fused, as it were, with the sarcolemma, we can readily comprehend, under this theory, how the simultaneous contraction of all the fibres of a muscle is produced by stimulation of its motor nerve. This idea is expressed in the accompanying diagram.

[1] MAREY, *Du mouvement dans les fonctions de la vie*, Paris, 1868, p. 280.

Although this view of the physiological action of the muscular fibres is extremely probable, it cannot be assumed that it has been absolutely demonstrated; but it is certainly more satisfactory and better sustained by experimental facts than any theory that has hitherto been advanced.

Mechanism of prolonged Muscular Contraction.—By a voluntary effort we are able to produce a muscular contraction of a certain duration, and of a power, within certain limits, proportionate to the amount of force we may desire to produce; but after a certain time, the muscle becomes fatigued, and it may become exhausted to the extent that it will not respond to the normal stimulus. This is the kind of muscular action most interesting to us as physiologists.

The experiments of Marey seem to show precisely how far the nervous action that gives rise to a powerful and continuous muscular contraction can be imitated by electricity. Calling the movement produced by a single electric discharge, *secousse*, which we have translated by the word spasm, he calls the persistent contraction, tetanus. We shall adopt this name to distinguish persistent muscular action from the single contraction that we have just described.

It is a curious fact that a continued current of galvanic electricity passed through a nerve or a muscle does not induce muscular contraction; and it is only when the current is closed or broken that any action is observed. But if we employ statical electricity, a muscular spasm occurs at every discharge, proportionate, in some degree, to the power of the excitation. If the discharges be very frequently repeated, or if a galvanic current be applied, broken by an interrupting apparatus, the spasms follow each other in quick succession. In experimenting upon the muscles of the frog, with a registering apparatus, Marey has found that with a gradual increase in the rapidity of the electric shocks, the individual muscular spasms become less and less distinct, and that finally the contraction is permanent. His diagrams show

well-marked spasms under ten excitations per second, a more complete fusion of the different acts with twenty per second, and a complete fusion, or tetanus, with twenty-seven per second. When the contraction had become continuous that was an elevation in the line, showing increased power, as the excitations became more and more frequent.[1]

This is precisely the kind of contraction that occurs in the physiological action of muscles. Although the nervous force is not by any means identical with electricity, either the interrupted galvanic current or a series of statical discharges is capable of producing a muscular action very like that which is involved in voluntary movements. The observations of Marey, showing that the intensity of what he terms artificial tetanic contraction is in proportion to the rapidity with which the electric discharges succeed each other, are exceedingly interesting in their practical applications; and an important question at once arises regarding the nervous force that excites voluntary motion. Is this a series of discharges, as it were, producing a power of muscular contraction in exact proportion to their rapidity? In view of the experiments just cited, this theory is very probable; and it is certain that a rapid succession of electric discharges almost exactly simulates the normal action. That vibrations, more or less regular, actually occur in muscular contraction has been settled beyond a doubt by the researches of Wollaston, Haughton, and more lately by Helmholtz, the latter having recognized a musical tone in contracting muscles, exactly corresponding with the number of impressions per second made upon the nerve. He farther devised an ingenious method of recognizing the tone, by filling the ears with wax and contracting the temporal and masseter muscles. Marey has found, in repeating this experiment, that the tone may be changed by modifying the intensity of the muscular action. With the jaws feebly contracted, a grave sound is produced, and this can be raised

[1] MAREY, *op. cit.*, p. 373, *et seq*

one-fifth, by contracting the muscles as forcibly as possible.[1]

The nerves are not capable of conducting an artificial stimulus for an indefinite period, nor are the muscles able to contract for more than a limited time upon the reception of such an impression. The electric current may be made to destroy for a time both the nervous and muscular irritability; these properties becoming gradually extinguished, the parts becoming fatigued before they are completely exhausted. Precisely the same phenomena are observed in the physiological action of muscles. When a muscle is fatigued artificially, a tetanic condition is excited more and more easily, but the intensity of the contraction proportionally diminishes.[2] Muscles contracting in obedience to an effort of the will pass through the same stages of action. It is probable that constant contraction is excited more and more easily as the muscles become fatigued, because the nervous force gradually diminishes in intensity. It is certain that the vigor of contraction at the same time progressively diminishes.

Electric Phenomena in the Muscles.—It was ascertained a number of years ago, by Matteucci, that all living muscles are the seat of electric currents; not very powerful, it is true, but still sufficiently marked to be detected by ordinary galvanometers. It is difficult, in the present state of our knowledge, to appreciate the physiological significance of this fact, and we shall therefore merely allude to the chief electric phenomena that are ordinarily observed, without attempting to follow out the elaborate and curious experiments since made by Du Bois-Reymond and others. One of the most simple methods of demonstrating this current is to prepare the leg of a frog with the crural nerve attached, and apply one portion of the nerve to the deep parts of an incised muscle and the other to the surface. As soon as the connection is made, a contraction of the leg takes place.

[1] MAREY, *op. cit.*, p. 455. [2] Idem., p. 378, *et seq.*

The same fact may be demonstrated with an ordinary galvanometer; but the evidence obtained by the frog's leg, when the experiment is properly performed, is sufficiently conclusive.

Matteucci constructed out of the fresh muscles from the thigh of the frog, what is sometimes called a frog-battery; which exhibits these currents in the most striking manner, their intensity being in direct ratio to the number of elements in the pile. To do this, he takes the muscles of the lower half of the thigh from several frogs, removing the bones, and arranges them in a series, each with its conical extremity inserted into the central cavity of the one below. In this way the external surface of each thigh except the last is in contact with the internal surface of the one below. If the two extremities of the pile be now connected with a galvanometer, quite a powerful current from the internal to the external surface of the muscle may be demonstrated. In a pile formed of ten elements, the needle of a galvanometer was deviated to from 30° to 40°.[1]

Electric currents are observed in all living muscles, but are most marked in the mammalia and warm-blooded animals. They exist, also, for a certain time after death. Artificial tetanus of the muscles, however, instead of intensifying the current, causes the galvanometer to recede. If, for example, the needle of the instrument show a deviation of 30° during repose, when the muscle is excited to tetanic contraction, it will return so as to mark only 10° or 15°. This phenomenon is observed only during a continued muscular contraction, and does not attend a single spasm.

Muscular Effort.—The mere voluntary movement of parts of the body, when there is no obstacle to be overcome

[1] MATTEUCCI, *Leçons sur les phénomènes physiques des corps vivants*, Paris, 1847, p. 175, *et seq.* For a fuller exposition of these interesting phenomena, the reader is referred to the elaborate treatise on physiology, by Prof. Longet (*Traité de physiologie*, Paris, 1869, tome ii, pp. 620, 639).

or no great amount of force is required, is very different from a muscular effort. For example, in ordinary progression there is simply a movement produced by the action of the proper muscles, almost without our consciousness, and this is unattended with any modification in the circulation or respiration; but if we attempt to lift a heavy weight, to jump, to strike a powerful blow, or to make any vigorous effort, the action is very different. In the latter instance, we prepare for the muscular action by inflating the lungs, closing the glottis, and contracting more or less forcibly the expiratory muscles, so as to render the thorax rigid and unyielding; and by a concentrated effort of the will, the proper muscles are then brought into action.

This remarkable action of the muscles of the thorax and abdomen, due to simple effort, and independent of the particular muscular act that is to be accomplished, compresses the contents of the rectum and bladder, and obstructs very materially the venous circulation in the large vessels. It is well known that hernia is frequently produced in this way; the veins of the face and neck become turgid; the conjunctiva may become ecchymosed; and sometimes aneurismal sacs are ruptured. An effort of this kind is generally of short duration, and cannot, indeed, be prolonged beyond the time during which respiration can be conveniently arrested. At its conclusion there is commonly a prolonged expiration, which is audible and somewhat violent at its commencement.

There are degrees of effort which are not attended with this powerful action of the muscles of the chest and abdomen, and in which the glottis is not completely closed; and an opening into the trachea or larynx, rendering immobility of the thorax impossible, does not interfere with certain acts that require considerable muscular power. If we examine a dog with the glottis exposed, when he makes violent efforts to escape, we can see that the opening is firmly closed. This fact is indicated by Longet, and we have often observed it

in vivisections; but Longet has farther shown that dogs with an opening into the trachea are frequently able to run and leap with "astonishing agility." He also saw a horse, with a large canula in the trachea, that performed severe labor and drew heavily-loaded wagons in the streets of Paris.[1]

Passive Organs of Locomotion.

It would be out of place to describe fully and in detail all of the varied and complex movements produced by muscular action. Many of these, such as the movements of deglutition and of respiration, are necessarily considered in connection with the functions of which they form a part; but others are purely anatomical questions. Associated and antagonistic movements, automatic and reflex movements, etc., belong to the history of the motor nerves, and will be fully considered under the head of the nervous system.

The study of locomotion involves a knowledge of the physiological anatomy of certain passive organs, the bones, cartilages, and ligaments. Though a complete history of the structure of these parts trenches somewhat upon the domain of anatomy, we are tempted to give a brief description of their histology, as it will complete our account of the tissues of the body, with the exception of the nervous system and the organs of generation, which will be taken up hereafter.

Locomotion is effected by the muscles acting upon certain passive, movable parts. These are the bones, cartilages, ligaments, aponeuroses, and tendons. We have already described the fibrous structures, and it only remains for us to study the bones and cartilages.

Physiological Anatomy of the Bones.—The number, classification, and relations of the bones are questions belonging to descriptive anatomy; and the only points we propose to consider refer to their general or microscopic structure.

[1] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 669.

Every bone, be it long or short, is composed of what is called the fundamental substance, marked by microscopic cavities and canals of peculiar form. The cavities contain corpuscular bodies, called bone-corpuscles. The canals of larger size serve for the passage of blood-vessels, while the smaller canals (canaliculi) connect the cavities with each other, and finally with the vascular tubes. Many of the bones present a medullary cavity, filled with a peculiar structure, called marrow. In almost all bones there are two distinct portions: one, which is exceedingly compact, and the other, more or less spongy or cancellated. The bones are also invested with a membrane, containing vessels and nerves, called the periosteum.

The method usually employed in the study of the bones is by thin sections made in various directions, and examined either in their natural condition or with the calcareous matter removed by maceration in weak acid solutions. By the first method, we can make out the relations of the fundamental substance, the direction and relations of the vascular canals, and the form, size, relations, and connections of the bone-cavities and small canals. By the latter method we can isolate and study the organic and corpuscular elements.

Fundamental Substance.—This constitutes the true bony substance, the medullary contents, vessels, nerves, etc., being simply accessory. It is composed of a peculiar organic matter, called osteine, combined with various inorganic salts, in which the phosphate of lime largely predominates. In addition to the phosphate of lime, the bones contain carbonate of lime, fluoride of calcium, phosphate of magnesia, soda, and the chloride of sodium. The relative proportions of the organic and inorganic matters are somewhat variable; but the average is about one-third of the former to two-thirds of salts. This proportion is necessary to the proper consistence and toughness of the bones.

Anatomically, the fundamental substance is arranged in the form of regular, concentric lamellæ, about $\frac{1}{5000}$ of an

inch in thickness.[1] This matter is of an indefinitely and faintly striated appearance, but it cannot be reduced to distinct fibres. In the long bones the arrangement of the lamellæ is quite regular, surrounding the Haversian canals, and forming what are sometimes called the Haversian rods, following in their direction the length of the bone. In the short, thick bones the lamellæ are more irregular, frequently radiating from the central portion to the periphery. These peculiarities in the disposition of the fundamental substance will be more readily understood after a description of the Haversian canals.

Haversian Canals.—These canals exist in the compact bony structure. They are absent, or very rare, in the spongy and reticulated portions. Their form is rounded or ovoid, the larger ones being sometimes quite irregular. In the long bones their direction is generally longitudinal, although they anastomose by lateral branches. Each one of these canals contains a blood-vessel, and their disposition constitutes the vascular arrangement of the bones. They are all connected with the opening on the surface of the bones, by which the arteries penetrate and the veins emerge. Their size, of course, is variable. According to Sappey, the largest are about $\frac{1}{60}$ and the smallest $\frac{1}{800}$ of an inch in diameter. Their average size is from $\frac{1}{250}$ to $\frac{1}{200}$ of an inch.[2] In a transverse section of a long bone the Haversian canals may be seen cut across and surrounded by from twelve to fifteen lamellæ. In a longitudinal section the course and anastomoses may be studied.

Lacunæ.—The fundamental substance is everywhere marked by irregular, microscopic excavations, of a peculiar form, called lacunæ, or osteoplasts. These were at one time supposed to be corpuscles of calcareous matter, and were known as the bone-corpuscles; but it has since been ascertained that this appearance is due to the imperfect methods

[1] SAPPEY, *Traité d'anatomie*, Paris, 1866, tome i., p. 84.

[2] SAPPEY, *op. cit.*, p. 76.

of preparation of the thin sections of bone. They are connected with numerous little canals, giving them a stellate appearance. These are most numerous at the sides. The lacunæ measure from $\frac{1}{1250}$ to $\frac{1}{800}$ of an inch in their long diameter, by about $\frac{1}{2500}$ of an inch in width.[1] They contain the true bone-corpuscles, which we will presently describe.

Canaliculi.—These are little wavy canals, connecting the lacunæ with each other and presenting a communication between the first series of lacunæ and the Haversian canals. Each osteoplast presents from eighteen to twenty canaliculi radiating from its borders. Their length is from $\frac{1}{800}$ to $\frac{1}{500}$ of an inch, and their diameter about $\frac{1}{25000}$ of an inch.[2] The arrangement of the Haversian canals, lacunæ, and canaliculi is shown in Fig. 19.

FIG. 19.

Vascular canals and lacunæ, seen in a transverse section of the diaphysis of the humerus. Magnified two hundred diameters.—1, 1, 1, Section of the Haversian canals; 2, section of a longitudinal canal divided at the point of its anastomosis with transverse canal. Around the canals, cut across perpendicularly, are seen the lacunæ (with their canaliculi), forming concentric rings. (SAPPEY, *Traité d'anatomie*, Paris, 1866, tome i., p. 79.)

Bone-cells or Corpuscles.—By treating perfectly-fresh specimens of bone with weak acid solutions, Virchow has

[1] SAPPEY, *op. cit.*, p. 80. [2] Idem., p. 81.

demonstrated the presence of stellate cells, or corpuscles, exactly filling up the lacunæ, and sending prolongations into the canaliculi.[1] These structures have since been studied by Rouget, who has succeeded in demonstrating them in fresh bones from the fœtus, without using any reagent.[2] They are stellate, granular, with a large nucleus and several nucleoli, and are of exactly the size and form of the lacunæ. They send out prolongations into the canaliculi, but it has been impossible to ascertain positively whether or not they form membranes lining the canaliculi through their entire length.

Marrow of the Bones.—The peculiar structure called marrow is found in the medullary cavities of the long bones, filling them completely and moulded to all the irregularities of their surface. It is also found filling the cells of the spongy portion. In other words, with the exception of the vascular canals, lacunæ, and canaliculi, the marrow fills all the spaces in the fundamental substance. We know very little of the functions of the marrow, we shall therefore pass it over with a brief description.

It is now settled that the cavities of the bones are not lined with a membrane corresponding to the periosteum, and that the marrow is applied directly to the bony substance. In the fœtus and in very young children, the marrow is red and very vascular. In the adult it is yellow in some bones, and gray or gelatiniform in others. It contains certain peculiar cells and nuclei, with amorphous matter, adipose vesicles, connective tissue, blood-vessels, and nerves.

Medullocells.—Robin has described little bodies, existing both in the form of cells and free nuclei, called medullocells. These are found in greater or less number in the bones at

[1] VIRCHOW, *Cellular Pathology*, Philadelphia, 1863, p. 112. Virchow's first observations were made in 1850.

[2] ROUGET, *Note sur les corpuscles des os.*—*Journal de la physiologie*, Paris, 1858, tome i., p. 764, *et seq.*

all ages, but are more abundant in proportion as the amorphous matter and fat-cells are deficient. The nuclei are spherical, with borders sometimes irregular, generally without nucleoli, finely granular, and from $\frac{1}{5000}$ to $\frac{1}{3000}$ of an inch in diameter. They are insoluble in acetic acid.[1] The cells are less numerous than the free nuclei. They are spherical or slightly polyhedric, contain a few pale granulations, are rendered pale, but are not dissolved by acetic acid, and measure about $\frac{1}{1700}$ of an inch in diameter.[2]

Myeloplaxes.—These are irregular, nucleated patches, also described by Robin, more abundant in the spongy portions of the bones than in the medullary canals, and are applied to the internal surfaces of the bones. They are exceedingly irregular in size and form (measuring from $\frac{1}{1200}$ to $\frac{1}{250}$ of an inch in diameter), are finely granular, and present from two to twenty or thirty nuclei. The nuclei are clear, ovoid, generally with a nucleolus, and are from $\frac{1}{2800}$ to $\frac{1}{2500}$ of an inch long, by $\frac{1}{5000}$ to $\frac{1}{4000}$ of an inch broad. The myeloplaxes are rendered pale by acetic acid, and the nuclei are then brought out more distinctly.[3]

In addition to the anatomical elements just described, the marrow contains a few very delicate bundles of connective tissue, most of which accompany the blood-vessels. In the fœtus the adipose vesicles are few or may be absent; but in the adult they are quite numerous, and in some bones seem to constitute the whole mass of the marrow. They do not differ materially from the fat-cells in other situations. Holding these different structures together, is a variable quantity of semitransparent, amorphous, or slightly granular matter.

The nutrient artery of the bones sends branches to the marrow, generally two in number for the long bones, which are distributed between the various anatomical elements, and

[1] Littré et Robin, *Dictionnaire de médecine*, Paris, 1865, Article, *Médullocelle.*

[2] Pouchet, *Précis d'histologie humaine*, Paris, 1864, p. 106.

[3] Littré et Robin, *Dictionnaire de médecine*, Paris, 1865, Article, *Myéloplaxe.*

finally surround the fatty lobules and the fat-vesicles with a delicate capillary plexus. The veins correspond to the arteries in their distribution. The nerves follow the arteries, and are lost when these vessels no longer present a muscular coat.[1] Nothing is known of the presence of lymphatics in any part of the bones, or in the periosteum.

The only point of physiological interest connected with the marrow is, that it has been found to possess, in common with the periosteum, but in a less degree, the property of generating true bony substances. We shall see farther on, that the periosteum is not only very important to the nutrition of the bones, but that it will generate bone when transplanted into vascular parts. M. Ollier, who has made a very extended series of experiments upon the physiological properties of the periosteum, endeavored to produce bone by transplanting portions of marrow, but was unsuccessful. M. Goujon, however, has lately been more fortunate. He has found that frequently, but not always, marrow transplanted into the muscular tissue will generate bone, particularly the marrow taken from young bones, but the bony tissue thus formed is soon absorbed.[2]

Periosteum.—In most of the bones the periosteum presents a single layer of fibrous tissue; but in some of the long bones two or three layers may be demonstrated. This membrane adheres to the bone, but can generally be separated without much difficulty. It covers the bones completely, except at the articular surfaces, where its place is supplied by cartilaginous incrustation. It is composed mainly of fibres of the white inelastic variety, with numerous small elastic fibres, blood-vessels, nerves, and a few adipose vesicles.

The arterial branches ramifying in the periosteum are

[1] SAPPEY, *op. cit.*, p. 95.

[2] GOUJON, *Recherches expérimentales sur les propriétés physiologiques de la moelle des os.—Journal de l'anatomie*, Paris, 1869, tome vi., p. 399, *et seq.*

quite numerous, forming a close, anastomosing plexus, which sends numerous small branches into the bony substance. There is nothing peculiar in the arrangement of the veins. The distribution of the veins in the bony substance has been very little studied.

The nerves of the periosteum are very abundant, and form in its substance quite a close plexus.

The adipose tissue is very variable in quantity. In some parts it forms a continuous sheet, and in others the vesicles are scattered here and there through the substance of the membrane.

The importance of the periosteum to the nutrition of the bones is very great. Instances are on record where bones have been removed, leaving the periosteum, in which the entire bone has been regenerated. The importance of the periosteum has been still farther illustrated by the remarkable experiments of M. Ollier, upon transplantation of this membrane in the different tissues of living animals.[1]

Physiological Anatomy of Cartilage.—In this connection the structure of the articular cartilages presents the chief physiological interest. The articular surfaces of all the bones are encrusted with a layer of cartilage, varying in thickness from $\frac{1}{50}$ to $\frac{1}{25}$ of an inch. The cartilaginous substance is white, opaline, and semitransparent when examined in thin sections. It is not covered with any membrane, but in the non-articular cartilages it has an investment analogous to the periosteum.

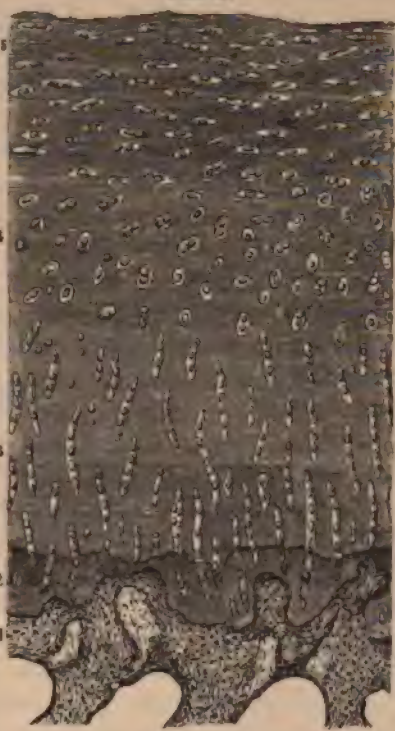
Examined in thin sections, cartilage is found to consist of a homogeneous fundamental substance, marked with numerous excavations, called cartilage-cavities, or chondroplasts. The intervening substance has a peculiar organi-

[1] The original memoirs of M. Ollier were published in the *Journal de la physiologie*, Paris, 1859–1863, tome ii., pp. 1, 169, 468, tome iii., p. 88, tome iv., p. 87, tome v., p. 59, and tome vi., pp. 466, 517. He has since published an elaborate work on the subject, in two volumes. (*Traité expérimentale et clinique de la génération des os*, Paris, 1867.)

base, called cartilagine. By prolonged boiling this is changed into a new substance, called chondrine. The organic matter is united with a certain proportion of inorganic salts. This fundamental substance is elastic and resisting. The cartilages are closely united to the subjacent bony tissue. The free articular surface has already been described.[1]

Cartilage-Cavities.—These cavities are rounded or ovoid, measuring from $\frac{1}{1250}$ to $\frac{1}{300}$ of an inch in diameter.[2] They are generally smaller in the articular cartilages than in other situations, as in the costal cartilages. They are simple excavations in the fundamental substance, have no lining membrane, and contain a small quantity of a viscid liquid, with one or more cells. They are entirely analogous to the lacunæ of the bones.

FIG. 20.



Perpendicular section of a diarthrodial cartilage; 1, 1, Osseous tissue; 2, 2, superficial layer of osseous tissue treated with hydrochloric acid; 3, 3, cavities and cells of the deep layer of cartilage; 4, 4, cavities and cells of the middle layer; 5, 5, cavities and cells of the superficial layer. (SAPPEY, *Traité d'anatomie*, Paris, 1867, tome i., p. 452.)

Cartilage-Cells.—Near the surface of the articular cartilages the cavities contain each a single cell; but in the deeper portions the cavities are long and contain from two to twenty cells arranged longitudinally. The cells are of about the size of the smallest

[1] See page 40. [2] POUCHET, *Précis d'histologie humaine*, Paris, 1864, p. 117.

cavities. They are ovoid, with a large, granular nucleus. They often contain a few small globules of oil. In the costal cartilages the cavities are not numerous, but are rounded and quite large. The cells contain generally a certain amount of fatty matter. The appearance of the ordinary articular cartilage is represented in Fig. 20.

The ordinary cartilages have neither blood-vessels, lymphatics, nor nerves, and are nourished exclusively by imbibition from the surrounding parts. Their function has already been sufficiently considered in treating of the synovial membranes. In the development of the body, the anatomy of the cartilaginous tissue possesses peculiar interest, from the fact that the deposition of cartilage precedes the formation of bone; but we have here only to do with the permanent cartilages.

Fibro-Cartilage.—This variety of cartilage presents certain important peculiarities in the structure of its fundamental substance. It exists in the synchondroses, the cartilages of the ear, of the Eustachian tubes, the interarticular disks, the intervertebral cartilages, the cartilages of Santorini and of Wrisberg, and the epiglottis. Its structure has been very closely and successfully studied by Sappey, who has arrived at results differing considerably from those obtained by other observers.

According to Sappey,[1] the fibro-cartilage is composed of true fibrous tissue with a great predominance of elastic fibres, fusiform, nucleated fibres, a certain number of adipose vesicles, cartilage-cells, and numerous blood-vessels and nerves. The presence of cartilage-cells assimilates this tissue to the ordinary cartilage, though its structure is very much more complex. The fibrous elements above mentioned take the place of the homogeneous fundamental substance of the true cartilage. The most important peculiarity in the structure of this tissue is that it is abundantly supplied with blood-vessels and nerves.

[1] SAPPEY, *Traité d'anatomie*, Paris, 1867, tome i., p. 458, *et seq.*

The reader is referred to works upon anatomy for a history of the action of the muscles. In some works upon physiology, will be found descriptions of the acts of walking, running, leaping, swimming, etc.; but we have thought it better to omit these subjects, rather than to enter as minutely as would be necessary into anatomical details, and to give elaborate descriptions of movements, so simple and familiar.

CHAPTER XVII.

VOICE AND SPEECH.

Sketch of the physiological anatomy of the vocal organs—Vocal chords—Muscles of the larynx—Crico-thyroid muscles—Arytenoid muscle—Lateral crico-arytenoid muscles—Thyro-arytenoid muscles—Mechanism of the production of the voice—Appearance of the glottis during ordinary respiration—Movements of the glottis during phonation—Variations in the quality of the voice, depending upon differences in the size and form of the larynx and the vocal chords—Action of the intrinsic muscles of the larynx in phonation—Action of the accessory vocal organs—Mechanism of the different vocal registers—Mechanism of speech.

THERE are few subjects connected with human physiology of greater interest than the mechanism of voice and speech. In common with most of the higher classes of animals, man is endowed with voice; but, in addition, he is able to express, by speech, the ideas that are the result of the working of the brain. In this regard there is a difference between man and all other animals. It is the remarkable development and the peculiar properties of the brain that enable him to acquire the series of movements that constitute articulate language; and this faculty is always impaired *pari passu* with deficiency in the intellectual endowment. Language is one of the chief expressions of intelligence; and its study, in itself, constitutes almost a distinct science, inseparably connected with psychology. In connection with the study of movements, therefore, it is not necessary to discuss the origin and construction of language, but simply to indicate the mechanism, first, of the formation of the voice, and

afterward the manner in which the voice is modified so as to admit of the production of articulate sounds.

The voice in the human subject, presenting, as it does, a variety of characters as regards intensity, pitch, and quality, and susceptible of great modifications by habit and cultivation, affords a very extended field for physiological study. Of late years this has been the subject of careful investigation by the most eminent physicists and physiologists; but to follow it out to its extreme limits requires a knowledge of the physics of sound and the theory of music, a full consideration of which would be inconsistent with the scope and objects of this work. We shall content ourselves, therefore, with a sketch of the physiological anatomy of the parts concerned in the formation of the voice, and the mechanism by which sounds are produced in the larynx, without treating fully of their varied modifications in quality. It will not be necessary to treat of the different theories of the voice that have been presented from time to time, except in so far as they have been confirmed by more recent and complete observations, particularly those in which the vocal organs have been studied in action by means of the laryngoscope.

Sketch of the Physiological Anatomy of the Vocal Organs.

The principal organ concerned in the production of the voice is the larynx. The accessory organs are the lungs, trachea, and expiratory muscles, and the mouth and resonant cavities about the face. The lungs furnish the air by which the vocal chords are thrown into vibration, and the mechanism of this action is only a modification of the process of expiration. By the action of the expiratory muscles the intensity of vocal sounds is regulated. The trachea not only conducts the air to the larynx, but, by certain variations in its length and caliber, may assist in modifying the pitch of the voice. Most of the variations in the tone and quality, however, are effected by the action of the larynx itself and the parts situated above it.

It is impossible to give a complete account of the structure of the larynx, without going more fully than is desirable into purely anatomical details. Some anatomical points have already been referred to under the head of respiration, in connection with the respiratory movements of the glottis;[1] and we propose here only to refer to the situation of the vocal chords, and to indicate the modifications that they can be made to undergo in their relations and tension by the action of certain muscles.

The vocal chords are stretched across the superior opening of the larynx from before backward. They consist of two pairs. The superior, called the false vocal chords, are not concerned in the production of the voice. They are less prominent than the inferior chords, though they have nearly the same direction. They are covered by an excessively-thin mucous membrane, which is closely adherent to the sub jacent tissue. The chords themselves are composed of fibres of the white inelastic variety, mixed with a few elastic fibres.

The true vocal chords are situated just below the superior chords. Their anterior attachments are near together, at the middle of the thyroid cartilage, and are immovable. Posteriorly they are attached to the movable arytenoid cartilages; and by the action of certain muscles, their tension may be modified, and the chink of the glottis may be opened or closed. These ligaments are much larger than the false vocal chords, and contain a very great number of elastic fibres. Like the superior ligaments, they are covered with an excessively-thin and closely-adherent mucous membrane. According to M. Fournié, the author of a very elaborate and recent work on the voice, the mucous membrane over the borders of the chords is covered with pavement-epithelium, without cilia.[2] There are no mucous glands in the membrane covering either the superior or the inferior chords.

[1] See vol. i., Respiration, p. 358.

[2] Fournié, *Physiologie de la voix et de la parole*, Paris, 1866, p. 129.

It has been conclusively shown, particularly by the experiments of Longet, that the inferior vocal chords are alone concerned in the production of the voice. This author, who has made numerous experiments on phonation, has demonstrated, by operations on dogs, that the epiglottis, the superior vocal chords, and the ventricles of the larynx, may be injured, without producing any serious alteration in the voice; but that phonation becomes impossible after serious lesion of the inferior chords.[1] This being the fact, as far as the mere production of the voice in the larynx is concerned, we have only to study the mechanism of the action of the inferior ligaments and the muscles by which their tension and relations are modified.

Muscles of the Larynx.—Anatomists usually divide the muscles of the larynx into extrinsic and intrinsic. The extrinsic muscles are attached to the outer surface of the larynx and to adjacent organs, such as the hyoid bone and the sternum. They are concerned chiefly in its movements of elevation or depression. The intrinsic muscles are attached to the different parts of the larynx itself, and, by their action upon the articulating cartilages, are capable of modifying the condition of the vocal chords. The number of the intrinsic muscles is nine, four pairs and a single muscle. In studying the situation and attachments of these muscles, it will be useful at the same time to note their mode of action. This has been experimentally demonstrated by Longet, who has studied the isolated action of the different muscles by galvanizing the nervous filament distributed to each one, either in the living animal, or in animals recently killed. In this way he has been able to show the mechanism of dilatation of the larynx during inspiration, and to indicate the precise action by which the vocal chords are rendered tense or are relaxed.[2] These experiments, by the positive charac-

[1] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 728, *et seq.*

[2] *Op. cit.*, p. 727.

ter of their results, have done much to simplify the study of the muscular acts concerned in the production of the voice.

Bearing in mind the relations and attachments of the vocal chords, we can understand precisely how they can be rendered tense or loose by muscular action. Their fixed point is in front, where their extremities, attached to the thyroid cartilage, are nearly or quite in contact with each other. The arytenoid cartilages, to which they are attached posteriorly, present a movable articulation with the cricoid cartilage; and the cricoid, narrow in front, and wide behind, where the arytenoid cartilages are attached, presents a movable articulation with the thyroid cartilage. It is evident, therefore, that muscles acting upon the cricoid cartilage can cause it to swing upon its two points of articulation with the inferior cornua of the thyroid, raising the anterior portion and approximating it to the lower edge of the thyroid; and, as a consequence, the posterior portion, which carries the arytenoid cartilages and the posterior attachments of the vocal chords, is depressed. This action would, of course, increase the distance between the arytenoid cartilages and the anterior portion of the thyroid, elongate the vocal chords, and subject them to a certain degree of tension. Experiments have shown that such an effect is produced by the contraction of the crico-thyroid muscles.

The articulations of the different parts of the larynx are such that the arytenoid cartilages may be approximated to each other posteriorly, though perhaps only to a slight extent, thus diminishing the interval between the posterior attachments of the vocal chords. This action can be effected by contraction of the single muscle of the larynx, the arytenoid, and also by the lateral crico-arytenoid muscles. The thyro-arytenoid muscles, the most complicated of all the intrinsic muscles in their attachments and the direction of their fibres, according to Longet, give rigidity and increased capacity of vibration to the vocal chords.[1]

[1] *Op. cit.*, p. 730.

The posterior crico-arytenoid muscles, arising from each lateral half of the posterior surface of the cricoid cartilage, passing upward and outward to be inserted into the outer angle of the inferior portion of the arytenoid cartilages, rotate these cartilages outward, separate them, and act as dilators of the chink of the glottis. These muscles are chiefly concerned in the respiratory movements during inspiration.

The muscles mainly concerned in the modifications of the voice by their action upon the vocal chords are the crico-thyroids, the arytenoid, the lateral crico-arytenoids, and the thyro-arytenoids. The following is a sketch of their attachments and mode of action:

Crico-thyroid Muscles.—These muscles are situated on the outside of the larynx at the anterior and lateral portions of the cricoid cartilage. Each muscle is of a triangular form, the base of the triangle looking posteriorly. It arises from the anterior and lateral portions of the cricoid cartilage, and its fibres diverge to be inserted into the inferior border of the thyroid cartilage, extending from the middle of this border posteriorly, as far back as the inferior cornua. Longet, after dividing the nervous filaments distributed to these muscles, noted hoarseness of the voice, depending upon relaxation of the vocal chords; and by imitating its action mechanically, he approximated the cricoid and thyroid cartilages in front, carried back the arytenoid cartilages, and rendered the chords tense.[1]

Arytenoid Muscle.—This single muscle fills up the space between the two arytenoid cartilages and is attached to their posterior surface and borders. Its evident action is to approximate the posterior extremities of the chords and constrict the glottis, as far as the articulations of the arytenoid cartilages with the cricoid will permit. In any event, this muscle is important in phonation, as it serves to fix the posterior attachments of the vocal chords and

[1] LONGET, *loc. cit.*

to increase the efficiency of certain of the other intrinsic muscles.[1]

Lateral Crico-arytenoid Muscles.—These muscles are situated in the interior of the larynx. They arise from the sides and superior borders of the cricoid cartilage, pass upward and backward, and are attached to the base of the arytenoid cartilages. By dividing all of the filaments of the recurrent laryngeal nerves except those distributed to these muscles, and then galvanizing the nerves, Longet has shown that they act to approximate the vocal chords and constrict the glottis, particularly in its interligamentous portion.[2] These muscles, with the arytenoid, act as constrictors of the larynx.

Thyro-arytenoid Muscles.—It is sufficiently easy to indicate the relations and attachments of these muscles, but their mode of action is more complex and difficult of comprehension. When we come to study the conditions of the vocal chords involved in certain modifications of the voice, we shall refer more in detail to the action of different fasciculi of these muscles. In this connection we shall only describe very briefly their situation and attachments, and the general results of their contraction.

The thyro-arytenoid muscles are situated within the larynx. They are broad and flat, and arise in front from the upper part of the crico-thyroid membrane and the lower half of the thyroid cartilage. From this line of origin, each muscle passes backward in two fasciculi, both of which are attached to the anterior surface and outer border of the arytenoid cartilages. The application of galvanism to the nervous filaments distributed to these muscles has the effect

[1] A very interesting case of aphonia, reported by Dr. Knight, of Boston, in which the appearances were carefully studied with the laryngoscope, seems to show that the arytenoid muscle is not capable of producing any considerable amount of movement, in totality, of the arytenoid cartilages. (KNIGHT, *Two Cases of Paralysis of Intrinsic Muscles of the Larynx.—Boston Medical and Surgical Journal*, 1869, New Series, vol. iii., p. 49, *et seq.*)

[2] LONGET, *loc. cit.*

of rendering the vocal chords rigid and increasing the intensity of their vibrations.[1] The great variations that may be produced in the pitch and quality of the voice by the action of muscles operating directly or indirectly on the vocal chords render the problem of determining the precise mode of action of the intrinsic muscles of the larynx exceedingly complicated and difficult. It is certain, however, that, in these muscular acts, the thyro-arytenoids play an important part. Their contraction regulates the thickness and rigidity of the vocal chords, while at the same time it modifies their tension. Fournié regards the swelling of the chords, which may be rendered regular and progressive under the influence of the will, as one of the most important agents in the formation of the tones of the voice.[2]

Mechanism of the Production of the Voice.

It will save much unprofitable discussion to dismiss quite briefly most of the theories that have been advanced to explain the production of the voice, and to avoid comparisons of the larynx with different kinds of musical instruments. Before the larynx had been studied in action by means of the laryngoscope, physiologists, having the anatomical structure of the parts for their only guide, presented various speculations with regard to the mechanism of phonation, which were frequently utterly opposed to each other in principle. The vocal apparatus was compared to wind or brass instruments, to reed-instruments, to string-instruments, to the flute, etc., and some even refused to the vocal chords any share in the sonorous vibrations. An apparatus was devised to imitate the vocal organs, experiments were made with the larynx removed from the body, and every thing seemed to be done, except to observe the organs in actual function.[3]

[1] LONGET, *op. cit.*, p. 730.

[2] FOURNIÉ, *Physiologie de la voix et de la parole*, Paris, 1866, p. 121.

[3] Perhaps the most elaborate of the observations made before the discovery of the laryngoscope are those of J. Müller, who experimented very extensively

A short time, however, after the laryngoscope came into use, the larynx was examined during the production of vocal sounds. The true value of previous theories was then positively demonstrated; and while it has not been possible to settle all disputed points with regard to the precise mode of action of certain muscles, the appearances of the larynx itself during phonation and the results of the action of certain of the intrinsic muscles have been quite accurately described. One of the first elaborate series of investigations of the subject by means of the laryngoscope was made by Manuel Garcia.[1] These observations were chiefly directed to the changes of the glottis in singing, and were made by Garcia upon his own person. The essential points developed by these experiments have since been confirmed by Battaille,[2] and many other observers.

Appearance of the Glottis during Ordinary Respiration.—If the glottis be examined with the laryngoscope during ordinary respiration, the wide opening of the chink during inspiration, due to the action of the crico-arytenoid muscles, can be observed without difficulty. This action is effected by a separation of the posterior points of attachment of the vocal chords to the arytenoid cartilages. During ordinary expiration, none of the intrinsic muscles seem to act, and the larynx is entirely passive; while the air is gently forced out by the elasticity of the lungs and of the thoracic walls. But as soon as an effort is made to produce a vocal sound, the appearance of the glottis undergoes a remarkable change, and becomes modified in the most varied and interesting manner, with the different changes in pitch and intensity that

with artificial vocal apparatus and with the larynx itself removed from the body. Many of the ideas of Müller have been carried out by recent laryngoscopic researches (*Manuel de physiologie*, Paris, 1851, p. 127, *et seq.*).

[1] GARCIA, *Observations on the Human Voice.—Proceedings of the Royal Society*, London, 1856, vol. vii., p. 399, *et seq.*

[2] BATTAILLE, *Nouvelles recherches sur la phonation.—Comptes rendus*, Paris, 1861, tome lii., p. 716, *et seq.*

the voice can be made to assume. Although it is sufficiently evident that a sound may be produced, and even that words may be articulated with the act of inspiration, true and normal phonation is effected during expiration only. It is evident, also, that the inferior vocal chords are the only ones concerned in the act. The changes in the position and tension of the chords we shall study, first with reference to the general act of phonation, and afterward as the chords act in the varied modifications of the voice, as regards intensity, pitch, and quality.

Movements of the Glottis during Phonation.

It is somewhat difficult to observe with the laryngoscope all of the vocal phenomena, on account of the epiglottis, which hides a considerable portion of the vocal chords anteriorly, especially during the production of certain tones; but the patience and skill of Garcia enabled him to overcome most of these difficulties, and to settle, by autolaryngoscopy, the most important questions with regard to the movements of the larynx in singing. It is fortunate that these observations, which are models of scientific accuracy and the result of most persevering study, were made by one profoundly versed, theoretically and practically, in the knowledge of music, and possessed of great control over the vocal organs.[1]

Garcia, after having observed the respiratory movements of the larynx, as we have briefly described them, noted that as soon as any vocal effort was made, the arytenoid cartilages were approximated, so that the glottis appeared as a narrow slit, formed by two chords of equal length, firmly attached posteriorly as well as anteriorly. The glottis thus

[1] Manuel Garcia, the author of these observations, is the son of Garcia, the great composer and singer, and the brother of Mme. Malibran. He now enjoys a great reputation in London, as a singing-master; and his experiments were made with a view, if possible, of reducing the art of singing, which had always been taught according to purely empirical methods, to scientific accuracy. It is evident that this could be accomplished only through an exact knowledge of the mechanism of the production of vocal sounds.

undergoes a marked change. A nearly passive organ, opening widely for the passage of air into the lungs, because the inspiratory act has a tendency to draw its edges together, and entirely passive in expiration, it has now become a sort of musical instrument, presenting a slit with borders capable of accurate vibration.

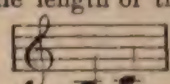
The approximation of the posterior extremities of the vocal chords and their tension by the action of certain of the intrinsic muscles are accomplished just before the vocal effort is actually made. The glottis being thus prepared for the emission of a particular sound, the expiratory muscles force air through the larynx with the required power. It seems wonderful how a carefully-trained voice can be modulated and varied in all its qualities, including the intensity of vibration, which is so completely under control; but when we consider the changes in its quality, we must remember, in explanation, the varying conditions of tension and length of the vocal chords, the differences in the size of the larynx, trachea, and vocal passages generally, and the different relations that the accessory vocal organs can be made to assume The power of the voice is simply due to the force of the expiratory act, which is regulated chiefly by the antagonistic relations of the diaphragm and the abdominal muscles. From the fact that the diaphragm, as an active inspiratory muscle, is exactly opposed to the muscles which have a tendency to push the abdominal organs, with the diaphragm over them, into the thoracic cavity, and thus diminish the pulmonary capacity, the expiratory and inspiratory acts can be balanced so nicely that the most delicate vocal vibrations can be produced. It is unnecessary to refer more in detail to the action of these muscles, as we have already treated of this subject fully in another volume.[1]

The glottis, thus closed as a preparation to a vocal act, presents a certain amount of resistance to the egress of air. This is overcome by the action of the expiratory muscles

[1] See vol. i., Respiration, p. 385, *et seq.*

and with the passage of air through the chink, the edges of the opening, which are formed by the true vocal chords, are thrown into vibration. Many of the different qualities that are recognized in the human voice are due to differences in the length, breadth, and thickness of the vibrating ribbons; but, aside from what is technically known as quality, the pitch is dependent chiefly upon the length of the opening through which the air is made to pass, and the degree of tension of the chords. The mechanism of these changes in the pitch of vocal sounds is well illustrated by Garcia in the following passage, which relates to what is known as the chest-voice:[1]

"If we emit veiled and feeble sounds, the larynx opens at the notes  do, re, mi., and we see the glottis agitated by large and loose vibrations throughout its entire extent. Its lips comprehend in their length the anterior apophyses of the arytenoid cartilages and the vocal chords; but, I repeat it, there remains no triangular space.

"As the sounds ascend, the apophyses, which are slightly rounded on their internal side, by a gradual apposition commencing at the back, encroach on the length of the glottis; and as soon as we reach the sounds  si, do., they finish by touching each other throughout their whole extent; but their summits are only solidly fixed one against the other at the notes  do, re.. In some organs these summits are a little vacillating when they form the posterior end of the glottis, and two or three half-tones which are formed show a certain want of purity and strength, which is very well known to singers. From  do, re. the vibrations, having become rounder and purer, are accomplished by the vocal ligaments alone, up to the end of the register.

[1] GARCIA, *op. cit.*, p. 401. We have indicated the notes in the following paragraphs by the method most commonly used by musicians, as is done by Mrs. Seiler, in the same quotation.

"The glottis at this moment presents the aspect of a line swelled toward its middle, the length of which diminishes still more as the voice ascends. We shall also see that the cavity of the larynx has become very small, and that the superior ligaments have contracted the extent of the ellipse to less than one-half."

These observations have been in the main confirmed by Battaille,[1] Emma Seiler,[2] and all who have applied the laryngoscope to the study of the voice in singing. A few years ago we had an opportunity of observing the changes in the form of the glottis during the production of vocal sounds of different degrees of pitch, through the kindness of Dr. Ephraim Cutter, of Boston. In these experiments the various points to which we have alluded were illustrated by autolaryngoscopy in the most marked manner; and nothing could be more striking than the changes in the form of the glottis in the transition from low to high notes. We have also frequently observed the general appearance of the glottis in phonation in experiments upon animals in which the glottis has been exposed to view.

Variations in the Quality of the Voice, depending upon differences in the Size and Form of the Larynx and the Vocal Chords.—We are all sufficiently familiar with the characters of the male as distinguished from the female voice, and what are known as the different vocal registers. In childhood, the general characters of the voice are essen-

[1] *Loc. cit.*

[2] Emma Seiler, *The Voice in Singing, translated from the German*, Philadelphia, 1868. This little work contains the results of a series of observations on the voice, made after the method employed by Garcia. These are peculiarly interesting, as they are applied particularly to the study of the female voice, and elucidate certain disputed points with regard to the production of the falsetto and the head-voice. The whole subject of the voice is treated in an eminently scientific manner, and the author professes to correct many faults in the methods of teaching the art of singing, that have had their origin in the employment of purely empirical methods.

tially the same in both sexes. The larynx is smaller than in the adult, and the vocal muscles are evidently more feeble; but the quality of the vocal sounds at this period of life is peculiarly pure and penetrating. While there are peculiarities that distinguish the voices of boys before the age of puberty, they present, as in the female, the different qualities of the soprano and contralto. At this age the voices of boys are capable of considerable cultivation, and their peculiar quality is sometimes highly prized in church-music. After the age of puberty, the female voice does not commonly undergo any very marked change, except in the development of additional strength and increased compass, the quality remaining the same; but in the male there is a rapid change at this time in the development of the larynx, and the voice assumes an entirely different quality of tone. This change does not usually take place if castration be performed in early life; and this barbarous operation was frequently resorted to in the seventeenth century, for the purpose of preserving the qualities of the soprano and contralto, particularly for church-music. It is only of late years, indeed, that this practice has fallen into disuse in Italy.

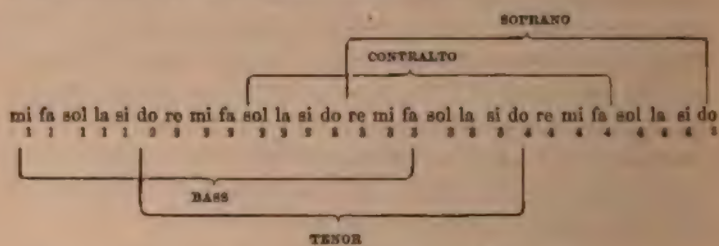
The ordinary range of all varieties of the human voice is given by Müller as equal to nearly four octaves; but it is rare that any single voice has a compass of more than two and a half octaves. There are examples, however, in which singers have acquired a compass of three octaves, and even more. The celebrated singer, Mme. Parepa-Rosa, has a compass of voice that touches three full octaves, from sol, to sol,. In music, the notes are written the same for the male as for the female voice, but the actual value of the female notes, as reckoned by the number of vibrations in the second, is always an octave higher than the male.[1]

In both sexes there are differences, both in the range and the quality of the voice, which it is impossible for a cultivated musical ear to mistake. In the male, we have the

[1] FOURNIÉ, *Physiologie de la voix et de la parole*, Paris, 1866, p. 531.

bass and the tenor, with an intermediate voice, called the barytone. In the female, we have the contralto and the soprano, with the intermediate, or mezzo-soprano. In the bass and barytone, the lower and middle notes are the most natural and perfect; and while the higher notes may be acquired by cultivation, they are not easy, and do not possess the same quality as the corresponding notes of the tenor. The same remarks apply to the contralto and soprano. The mezzo-soprano is regarded by many as an artificial division.

The following scale, proposed by Müller, gives the ordinary ranges of the different kinds of voice; but it must be remembered that there are individual instances in which these limits are very much exceeded:[1]



There is really no great difference in the mechanism of these different kinds of voice, and the differences in pitch are due chiefly to the greater length of the vocal chords in the low-pitched voices, and their shortness in the higher voices. The differences in quality are due to peculiarities in the conformation of the larynx, to differences in its size, and in the size and form of the auxiliary resonant cavities. Great changes in the quality of the voice may be effected by practice. A cultivated note, for example, has an entirely different sound from a harsh, irregular vibration; and, by practice, a tenor may imitate the quality of the bass, and *vice versa*, although the effort is unnatural. It is not at all unusual to hear male singers imitate very closely the notes

[1] Mueller, *Manuel de physiologie*, Paris, 1851, tome ii., p. 198.

of the female, and the contralto will sometimes imitate the voice of the tenor in a surprisingly natural manner. These facts have a somewhat important bearing upon certain disputed points with regard to the mechanism of the different vocal registers, which will be considered farther on.

Action of the Intrinsic Muscles of the Larynx in Phonation.—It is much more difficult to find an entirely satisfactory explanation of the different tones produced by the human larynx in the action of the intrinsic muscles than to describe the changes in the tension and relations of the vocal chords. These muscles are concealed from view, and the only idea that we can have of their action is by reasoning from a knowledge of their points of attachment, and by operations upon the dead larynx, either imitating the contraction of special muscles or galvanizing the nerves in animals recently killed. In this way, as we have seen, some of the muscular acts have been studied very satisfactorily; but the precise effect of the contraction of certain of the muscles, particularly the thyro-arytenoids, is still a matter of discussion.

In the production of low chest-tones, in which the vocal chords are elongated and at the minimum of tension that will allow of regular vibrations, the crico-thyroid muscles are undoubtedly brought into action, and are assisted by the arytenoid and the lateral crico-arytenoids, which combine to fix the posterior attachments of the vibrating ligaments. It will be remembered that the crico-thyroids, by approximating the cricoid and thyroid cartilages in front, have a tendency to remove the arytenoid cartilages from the anterior attachment of the chords.

As the tones produced by the larynx become higher in pitch, the posterior attachments of the chords are approximated more firmly, and at this time the lateral crico-arytenoids are probably brought into vigorous action.

The function of the thyro-arytenoids is more complex;

and it is probably in great part by the action of these muscles that the varied and delicate modifications in the rigidity of the vocal chords are produced.

The remarkable differences in singers in the purity of their tones are undoubtedly due in greatest part to the unswerving accuracy with which some put the vocal chords upon the stretch; while in those in whom the tones are of inferior quality, the action of the muscles is more or less vacillating, and the tension is frequently incorrect. The fact that some celebrated singers can make their voice heard above the combined sounds from a large chorus and orchestra is not due entirely to the intensity of the sound, but in a great measure to the absolute mathematical equality of the sonorous vibrations, and the comparative absence of discordant waves.[1] Musicians who have heard the voice of the celebrated basso, Lablache, all bear testimony to the remarkable quality of his voice, which could be heard at times above a powerful chorus and orchestra. A grand illustration of this occurred at the musical festival at Boston, in 1869. In some of the solos by Mme. Parepa-Rosa, accompanied by a chorus of nearly twelve thousand, with an orchestra of more than a thousand and largely composed of brass instruments, we distinctly heard the pure and just notes of this remarkable soprano, standing alone, as it were, against the entire choral and instrumental force; and this in an immense building containing an audience of forty thousand persons. The absolute accuracy of the tone was undoubtedly an important element in its remarkably penetrating

[1] Immense progress has been made in the analytical study of different sounds by the celebrated German physicist, Helmholtz. By means of his ingeniously-constructed resonators, taking advantage of the laws of consonance, in accordance with which the quality as well as the pitch of different tones is reproduced, he has been able to separate sounds into their different component parts as accurately as a ponderable compound is resolved into its constituent elements in the laboratory of the chemist.—(HELMHOLTZ, *Théorie physiologique de la musique fondée sur l'étude des sensations auditives*, Paris, 1868, p. 48, *et seq.*) This subject will be fully considered under the head of audition.

quality. In the same way we explain the fact that the flute, clarinet, or the sound from a Cremona violin, may be heard soaring above the chords of a full orchestra.

Action of the Accessory Vocal Organs.—A correct use of the accessory organs of the voice is of the greatest importance in singing; but the manner in which these parts perform their function is exceedingly simple, and does not require a very extended description. The human vocal organs, indeed, consist of a vibrating instrument, the larynx, and certain tubes and cavities by which the sound is reënforced and modified.

The trachea serves not only to conduct air to the larynx, but to reënforce the sound to a certain extent by the vibrations of the column of air in its interior. When a powerful vocal effort is made, it is easy to feel, with the finger upon the trachea, that the air contained in it is thrown into vibration. The structure of this tube is such that it may be elongated and shortened at will. In the production of low tones, the trachea is shortened and its caliber is increased, the reverse obtaining in the higher notes of the scale.

Coming to the larynx itself, we find that the capacity of its cavity is capable of certain variations. In fact, both the vertical and the bilateral diameters are diminished in the high notes and increased in low tones. The vertical diameter may be modified slightly by ascent and descent of the true vocal chords, and the lateral diameter may be reduced by the inferior constrictors of the pharynx, acting upon the sides of the thyroid cartilage.

The epiglottis, the superior vocal chords, and the ventricles are by no means indispensable to the production of vocal sounds. In the formation of high tones, the epiglottis is somewhat depressed, and the superior chords are brought nearer together; but this only affects the character of the resonant cavity above the glottis. In low tones the superior chords are separated. It was before the use of the

laryngoscope in the study of vocal phenomena that the epiglottis and the ventricles were thought to be so important in phonation. Undoubtedly the epiglottis has something to do with the character of the voice; but its function in this regard is not absolutely necessary, or even very important, as has been clearly shown by Longet in his experiments of excising the part in living animals.[1]

The most important modifications of the laryngeal sounds are produced by the resonance of air in the pharynx, mouth, and nasal fossæ. This resonance is indispensable to the production of the natural human voice. Under ordinary conditions, in the production of low notes the velum palati is fixed by the action of its muscular fibres, so that there is a reverberation of the bucco-pharyngeal and naso-pharyngeal cavities; that is, the velum is in such a position that neither the opening into the nose or the mouth is closed, and all of the cavities resound. As the tones are raised, the isthmus contracts, the part immediately above the glottis is also constricted, the resonant cavity of the pharynx and mouth is reduced in size, until finally, in the highest tones of the chest-register, the communication between the pharynx and the nasal fossæ is closed, and the sound is reënforced entirely by the pharynx and mouth. At the same time the tongue, a very important organ to singers, particularly in the production of high notes, is drawn back into the mouth. The point being curved downward, its base projects upward posteriorly, and assists in diminishing the capacity of the cavity. In the changes which the pharynx thus undergoes in the production of different tones, the uvula acts with the velum and assists in the closure of the different openings. In singing up the scale, this is the mechanism, as far as the chest-tones extend. When, however, we pass into what is known as the head-voice, the velum palati is drawn forward instead of backward, and the resonance takes place chiefly in the naso-pharyngeal cavity.

[1] LONGET, *Traité de physiologie*, Paris, 1869, tome ii., p. 727.

Mechanism of the different Vocal Registers.—There has been a great deal of discussion, even among those who have studied the voice with the laryngoscope, with regard to the exact mechanism of the different vocal registers. It is now pretty well settled how the ordinary tones of what is known as the chest-register are produced; but with regard to the falsetto, the difficulties in the way of direct observation are so great, that the question of its mechanism cannot be said to be definitively established.

The following are the vocal registers now recognized by most physiologists:

1. The chest-register, most powerful in male voices and in contraltos, and, indeed, almost characteristic of the male.

2. The falsetto register, which is the most natural voice of the soprano; though this voice is capable of chest-tones, not so full, however, as in the contralto or in the male. In the female this is known as the middle register.

3. The head-register, produced by a peculiar action of the glottis and the resonant cavities above the larynx. This is cultivated particularly in tenors and in the female.

Aside from the three registers, which belong to every voice, a practised ear can find no difficulty in distinguishing the different voices in nearly any part of the scale, both in the male and the female, by the following peculiarities: In the bass the low tones are full, natural, and powerful, and the higher tones nearly always seem more or less artificial. In singing, the passage from the natural to the artificial tones in the scale is generally more or less apparent. In the tenor the full, natural tones are higher in the scale, the lower tones being almost always feeble and wanting in roundness. Corresponding peculiarities enable us to distinguish between the contralto and the soprano.

Chest-Register.—We shall simply recapitulate briefly the mechanism of the chest-tones, to enable us to study more easily the transitions to the different upper registers. This

is the voice commonly used in speaking, and is the most natural, the vocal ligaments vibrating according to their tension, as the air is forced through the larynx from the chest, and the air in the pharynx, mouth, and nasal fossæ producing a resonance without any artificial division of the different cavities. As the tones are elevated the vocal chords are simply rendered more tense, and the parts above the larynx are more or less constricted, without any other change in the mechanism of the sound. But the chest-voice in the male cannot pass certain well-defined limits; and in the very highest notes it must be merged either into the head-voice or the falsetto. The falsetto, however, is now but little cultivated, though some tenor singers, after long practice, succeed in making the change from one register to the other so nicely that it is hardly perceptible, even to a cultivated ear. The head-voice has essentially the same mechanism in the male as in the female, and will be considered after we have discussed the falsetto, which is the natural voice of soprano singers.

Falsetto Register.—The difference of opinion among laryngoscopists with regard to the mechanism of the falsetto is probably in great part due to the fact that when these tones are produced, the isthmus of the fauces is so powerfully contracted that it becomes exceedingly difficult to study the action of the vocal chords. There is no reason for supposing that the mechanism of this register does not involve vibration of the true vocal chords, as in the chest-voice, the difference being in the tension and in the extent of the vibrating portion. According to the observations of Fournié, in the falsetto the tongue is pressed strongly backward and the epiglottis is forced over the larynx.[1] Mrs. Emma Seiler, from an extended series of autolaryngoscopic observations, has arrived at the conclusion that this voice involves vibrations of the fine, thin edges

[1] *Op. cit.*, p. 463.

of the chords only, a greater width vibrating in the production of the chest-voice. She is particularly careful to insist upon the distinction between the falsetto and the head-register, the latter being produced by an entirely different mechanism.[1] On the whole, this explanation seems to be the most satisfactory.

It must be remembered that the distinction between the chest-register or the head-register and the falsetto, as far as pitch is concerned, is not absolute. Certain of the high notes of the chest or the head-voice, for example, may be produced in the falsetto. In the cultivation of the female voice, Mrs. Seiler considers that it is exceedingly important not to strain the chest-voice to its highest point, but to use each register in its normal place in the scale, taking care, by practice, to render the transition from one to the other natural and agreeable. We have heard male singers, probably endowed with peculiar vocal powers, who were able, by the use of the falsetto, to imitate almost exactly the soprano voice, though without the sweetness and purity of tone characteristic of the perfect female organ. In the same way, by straining the chest-voice beyond its normal limits, some females, particularly contraltos, are able to produce a very good imitation of the tenor quality.

Head-Register.—This voice is highly cultivated, particularly in tenors and in the best female singers. It is not to be confounded, however, with the falsetto, as was done by some physiologists, before the invention of the laryngoscope.[2] Head-tones may be produced by cultivated male singers, bass and barytone, as well as tenor; but the former seldom have occasion for any but the chest-notes. Still, there are musical passages in which the *sotto-voce* head-notes of the bass have an exquisite softness, and are used with great effect. Mrs. Seiler has studied this voice by autolaryngo-

[1] EMMA SEILER, *The Voice in Singing*, Philadelphia, 1868, p. 56, *et seq.*

[2] MUELLER, *Manuel de physiologie*, Paris, 1851, tome ii., p. 199.

scopy with the greatest success, and has confirmed her views with regard to the mechanism of its production by numerous observations upon other singers. We have already stated that Fournié has shown that, in the transition to the head-voice, the velum palati is applied to the base of the tongue, and the sound is reënforced by resonance from the naso-pharyngeal cavity.[1] If this be its mechanism, its study with the laryngoscope must be exceedingly difficult.

The most important theory of the mechanism of the head-voice has been proposed by Mrs. Seiler. After long and patient effort, she was able to expose the glottis during the production of these tones, when it was found that the vocal chords were firmly approximated posteriorly, leaving an oval opening, with vibrating edges, involving only one-half or one-third of the vocal ligaments. This orifice contracted progressively with the higher tones. This peculiar division of the vocal ligaments is due, according to Mrs. Seiler, to the action of a muscular bundle, called the internal thyro-arytenoid, upon little cartilages, the cuneiform, extending forward from the arytenoid cartilage, in the substance of the vocal ligaments, as far as the middle of the glottis.[2]

With proper cultivation, the transition from the middle register to the head-voice in the female may be effected almost imperceptibly, thereby increasing the compass from three to six tones, and even more; and in the male the same may be accomplished without difficulty, particularly in tenors. There can be hardly any doubt of the fact that the naso-pharyngeal space is chiefly concerned in the resonance that takes place in head-tones, though its actual demonstration is very difficult. The distinction between the head and the chest-notes is fully as marked in the male as in the female; but it must be remembered that one of the great ends to be accomplished in the cultivation of the human voice is to make the three

[1] Fournié, *op. cit.*, p. 421. [2] *Op. cit.*, p. 60.

registers pass into each other so that they shall appear as one.[1]

Mechanism of Speech.

Articulate language consists in a conventional series of sounds made for the purpose of conveying certain ideas. There being no universal language, we must confine our description of the faculty of speech to the mode of production of the language in which this work is written. Language, as it is naturally acquired, is purely imitative, and does not involve of necessity the construction of an alphabet, with its combinations into syllables, words, and sentences; but as civilization has advanced, we have been taught to associate certain differences in the accuracy and elegance with which ideas are expressed, with the degree of development and cultivation of the intellectual faculties. Philologists have long since established a certain standard, varying, to some extent, it is true, with usage and the advance of knowledge, but still sufficiently definite, by which the correctness of modes of expression is measured. We do not propose to discuss the science of language, or to consider, in this connection, at least, the peculiar mental operations concerned in the expression of ideas, but to take our own tongue as we find it, and describe briefly the mechanism of the production of the most important articulate sounds.

Almost every language is imperfect, as far as an exact correspondence between its sounds and written characters is concerned. Our own language is full of incongruities in spelling, such as silent letters and arbitrary and unmeaning

[1] In studying the mechanism of the voice in singing, we have received great assistance in many practical points from Mme. Parepa-Rosa, to whose remarkable power as a vocalist we have already alluded, and Sig. A. Bendelari, of this city, the eminent singing-master. These distinguished artists, thoroughly skilled both in the science as well as the art of music, have elucidated several difficult questions, by their practical knowledge of the art of blending and modifying the different vocal registers.

variations in pronunciation; but these do not belong to the subject of physiology. There are, however, certain natural divisions of the sounds as expressed by the letters of the alphabet.

Vowels.—Certain articulate sounds are called vowel, or vocal, from the fact that they are produced by the vocal chords, and are but slightly modified as they pass out of the mouth. The true vowels, a, e, i, o, u, can all be sounded alone, and may be prolonged in expiration. These are the sounds chiefly employed in singing. The differences in their characters are produced by changes in the position of the tongue, mouth, and lips. The vowel-sounds are necessary to the formation of a syllable, and although they are generally modified in speech by consonants, each one may, of itself, form a syllable or a word. In the construction of syllables and words, the vowels have many different qualities, the chief differences being as they are made long or short. In addition to the modifications in the vowel-sounds by consonants, two or three may be combined so as to be pronounced by a single vocal effort, when they are called respectively, diphthongs and triphthongs. In the proper diphthongs, as oi, in voice, the two vowels are sounded. In the improper diphthongs, as ea, in heat, and in the Latin diphthongs, as æ, in Cæsar, one of the vowels is silent. In triphthongs, as eau, in beauty, only one vowel is sounded. Y, at the beginning of words, is usually pronounced as a consonant; but in other situations it is pronounced as e or i.

Consonants.—Some of the consonants have no sound in themselves, and only serve to modify vowel-sounds. These are called mutes. They are b, d, k, p, t, and c and g hard. Their office in the formation of syllables is sufficiently apparent.

The consonants known as semi-vowels are, f, l, m, n, r, s, and c and g soft. These have an imperfect sound of

themselves, approaching in character the true vowel-sounds. Some of these, l, m, n, and r, from the facility with which they flow into other sounds, are called liquids. Orthoepists have farther divided the consonants with reference to the mechanism of their pronunciation: d, j, s, t, z, and g soft, being pronounced with the tongue against the teeth, are called dentals; d, g, j, k, l, n, and q are called palatals; b, p, f, v, and m are called labials; m, n, and ng are called nasals; and k, q, and c and g hard are called gutturals.[1] After the full description we have given of the voice, it is not necessary to discuss farther the mechanism of these simple acts of articulation.

For the easy and proper production of articulate sounds, absolute integrity of the mouth, teeth, lips, tongue, and palate is required. We are all acquainted with the modifications in articulation, in persons in whom the nasal cavities resound unnaturally, from imperfection of the palate; and the slight peculiarities observed after loss of the teeth and in hare-lip are sufficiently familiar. The tongue is generally regarded, also, as an important organ of speech, and this is the fact in the great majority of cases; but instances are on record in which distinct articulation has been preserved after complete destruction of this organ.[2] These cases, however, are unusual, and do not invalidate the great importance of the tongue in ordinary speech.

It is thus seen that speech consists essentially in a modification of the vocal sounds by the accessory organs, or parts situated above the larynx; the latter being the true vocal instrument. While the peculiarities of pronunciation in different persons and the difficulty of acquiring foreign languages after the habits of speech have been formed show that the

[1] WORCESTER, *Dictionary of the English Language*, Boston, 1864, p. xvii.

[2] Numerous instances of preservation, more or less complete, of the faculty of speech after loss of the tongue, are quoted in works on physiology, among the most remarkable of which are those referred to by Dr. Elliotson (*Human Physiology*, London, 1840, p. 507).

organs of articulation must perform their function with great accuracy, their movements are simple, and vary with the peculiarities of different languages. The most interesting question, in its general physiological relations, is that to which the greatest part of this chapter has been devoted; and that is the mechanism of the production of the voice.

INDEX.

Elliot's Obstetric Clinic.

A Practical Contribution to the Study of Obstetrics and the Diseases of Women and Children. By GEORGE T. ELLIOT, Jr., A. M., M. D., Prof. of Obstetrics and the Diseases of Women and Children in the Bellevue Hospital Medical College, Physician to Bellevue Hospital and to the New York Lying-in Hospital, etc., etc. 8vo, pp. 458. . . Cloth, $4.50

This volume, by Dr. Elliot, is based upon a large experience, including fourteen years of service in the lying-in department of Bellevue Hospital of this city. The book has attracted marked attention, and has elicited from the medical press, both of this country and Europe, the most flattering commendations. It is justly believed that the work is one of the most valuable contributions to obstetric literature that has appeared for many years, and, being eminently practical in its character, cannot fail to be of great service to obstetricians.

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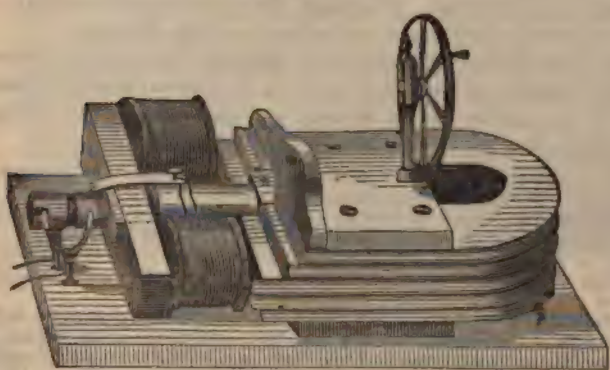

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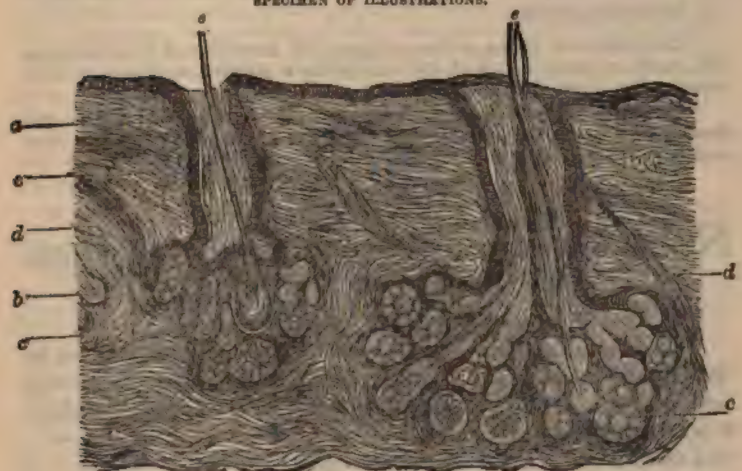

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